WEST Search History

ATE: Thursday, September 02, 2004

ide?	Set Name	Query	Hit Count
		DB=EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
☐	L8	L7 and l6	0
☐	L7	chelat$\|scaveng$|oxygen displacement gas|antiox$	81711
☐	L6	tfpi or tissue factor pathway inhibitor	111
		DB=PGPB,USPT; PLUR=YES; OP=ADJ	
☐	L5	20030108	10
☐	L4	L2 with l1	14
☐	L3	L2 same l1	30
☐	L2	chelat$\|scaveng$|oxygen displacement gas|antiox$	191083
☐	L1	tfpi or tissue factor pathway inhibitor	726

ND OF SEARCH HISTORY

side by side

		Count	Name result set
DB=PGPB,USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L1	(tfpi|tissue factor pathway inhibitor) same (antiox$\|chelat$|free radical|scaven$|nitrogen|helium|carbon dioxide|tocopherol)	39	L1

END OF SEARCH HISTORY

```
$%^STN;HighlightOn=  ***;HighlightOff=***  ;

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PASSWORD:
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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  May 12   EXTEND option available in structure searching
 NEWS  4  May 12   Polymer links for the POLYLINK command completed in REGISTRY
 NEWS  5  May 27   New UPM (Update Code Maximum) field for more efficient patent
                   SDIs in CAplus
 NEWS  6  May 27   CAplus super roles and document types searchable in REGISTRY
 NEWS  7  Jun 28   Additional enzyme-catalyzed reactions added to CASREACT
 NEWS  8  Jun 28   ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG,
                   and WATER from CSA now available on STN(R)
 NEWS  9  Jul 12   BEILSTEIN enhanced with new display and select options,
                   resulting in a closer connection to BABS
 NEWS 10  Jul 30   BEILSTEIN on STN workshop to be held August 24 in conjunction
                   with the 228th ACS National Meeting
 NEWS 11  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                   fields
 NEWS 12  AUG 02   CAplus and CA patent records enhanced with European and Japan
                   Patent Office Classifications
 NEWS 13  AUG 02   STN User Update to be held August 22 in conjunction with the
                   228th ACS National Meeting
 NEWS 14  AUG 02   The Analysis Edition of STN Express with Discover!
                   (Version 7.01 for Windows) now available
 NEWS 15  AUG 04   Pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover! will change September 1, 2004
 NEWS 16  AUG 27   BIOCOMMERCE: Changes and enhancements to content coverage
 NEWS 17  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                   status data from INPADOC
 NEWS 18  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS 19  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS 20  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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FILE 'HOME' ENTERED AT 10:23:43 ON 02 SEP 2004

=> file reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:23:51 ON 02 SEP 2004
```

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7
DICTIONARY FILE UPDATES: 31 AUG 2004 HIGHEST RN 736193-62-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

```
=> e tissue factor pathway inhibitor/cn
E1            1     TISSUE FACTOR (RAINBOW TROUT CLONE SSH39 GENE TF PRECURSOR)/
                    CN
E2            1     TISSUE FACTOR INHIBITOR/CN
E3            1 --> TISSUE FACTOR PATHWAY INHIBITOR/CN
E4            1     TISSUE FACTOR PATHWAY INHIBITOR (179-LEUCINE) (HUMAN PRECURS
                    OR)/CN
E5            1     TISSUE FACTOR PATHWAY INHIBITOR (ALANYL) (HUMAN)/CN
E6            1     TISSUE FACTOR PATHWAY INHIBITOR (DOG PRECURSOR)/CN
E7            1     TISSUE FACTOR PATHWAY INHIBITOR (HUMAN PRECURSOR)/CN
E8            2     TISSUE FACTOR PATHWAY INHIBITOR (HUMAN)/CN
E9            1     TISSUE FACTOR PATHWAY INHIBITOR (MOUSE STRAIN 129 GENE TFPIB
                    ETA ISOFORM .BETA. C-TERMINAL FRAGMENT)/CN
E10           1     TISSUE FACTOR PATHWAY INHIBITOR (SYNTHETIC 23-AMINO ACID C-T
                    ERMINAL FRAGMENT)/CN
E11           1     TISSUE FACTOR PATHWAY INHIBITOR (SYNTHETIC 30-AMINO ACID C-T
                    ERMINAL FRAGMENT)/CN
E12           1     TISSUE FACTOR PATHWAY INHIBITOR (SYNTHETIC 45-AMINO ACID C-T
                    ERMINAL FRAGMENT)/CN

=> s e3
L1            1 "TISSUE FACTOR PATHWAY INHIBITOR"/CN

=> d

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   194554-71-7  REGISTRY
CN   Proteinase inhibitor, TFPI (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Blood-coagulation factors, EPI (extrinsic pathway inhibitor)
CN   Blood-coagulation factors, LACI
CN   Blood-coagulation factors, lipoprotein-assocd. coagulation inhibitors
CN   Blood-coagulation factors, TFI
CN   EPI blood-coagulation factors
CN   Extrinsic pathway inhibitor blood-coagulation factors
CN   LACI blood-coagulation factors
CN   Lipoprotein-assocd. coagulation inhibitor
CN   Lipoprotein-assocd. coagulation inhibitors blood-coagulation factors
CN   Tissue factor inhibitor
CN     ***Tissue factor pathway inhibitor***
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, IPA, TOXCENTER, USPAT2, USPATFULL
DT.CA  CAplus document type:  Conference; Dissertation; Journal; Patent
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties);
       USES (Uses)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); PREP (Preparation); PROC (Process); PRP (Properties); RACT
       (Reactant or reagent); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
       (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents:  BIOL (Biological
```

```
       study); OCCU (Occurrence); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             600 REFERENCES IN FILE CA (1907 TO DATE)
              18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             603 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> sel l1 name
E1 THROUGH E11 ASSIGNED

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.76       7.97

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, AQUALINE, ANABSTR, ANTE,
       AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS,
       BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB,
       CROPU, DISSABS, DDFB, DDFU, DGENE, ...' ENTERED AT 10:25:35 ON 02 SEP 2004

74 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s e1-11 or 194554-71-7
         197   FILE ADISCTI
          18   FILE ADISINSIGHT
           9   FILE ADISNEWS
   3 FILES SEARCHED...
           4   FILE AGRICOLA
   6 FILES SEARCHED...
          15   FILE BIOBUSINESS
           9   FILE BIOCOMMERCE
           8   FILE BIOENG
        1264   FILE BIOSIS
  12 FILES SEARCHED...
          43   FILE BIOTECHABS
          43   FILE BIOTECHDS
         469   FILE BIOTECHNO
  15 FILES SEARCHED...
          16   FILE CABA
         124   FILE CANCERLIT
  17 FILES SEARCHED...
        1179   FILE CAPLUS
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  19 FILES SEARCHED...
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          40   FILE CONFSCI
  22 FILES SEARCHED...
  24 FILES SEARCHED...
           8   FILE DISSABS
  26 FILES SEARCHED...
         363   FILE DDFU
         630   FILE DGENE
  28 FILES SEARCHED...
  30 FILES SEARCHED...
          12   FILE IMSDRUGNEWS
         403   FILE DRUGU
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           6   FILE IMSRESEARCH
          14   FILE EMBAL
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        1306   FILE EMBASE
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         439   FILE ESBIOBASE
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          29   FILE FEDRIP
  39 FILES SEARCHED...
           1   FILE FROSTI
           1   FILE FSTA
         312   FILE GENBANK
           1   FILE HEALSAFE
         103   FILE IFIPAT
  44 FILES SEARCHED...
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        67   FILE JICST-EPLUS
  47 FILES SEARCHED...
        53   FILE LIFESCI
      1003   FILE MEDLINE
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  52 FILES SEARCHED...
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       613   FILE PASCAL
  55 FILES SEARCHED...
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         9   FILE PHARMAML
        23   FILE PHIN
        51   FILE PROMT
  61 FILES SEARCHED...
        19   FILE PROUSDDR
      1235   FILE SCISEARCH
  64 FILES SEARCHED...
       435   FILE TOXCENTER
       595   FILE USPATFULL
  67 FILES SEARCHED...
        34   FILE USPAT2
  69 FILES SEARCHED...
         1   FILE VETU
  71 FILES SEARCHED...
       103   FILE WPIDS
  73 FILES SEARCHED...
       103   FILE WPINDEX

  48 FILES HAVE ONE OR MORE ANSWERS,   74 FILES SEARCHED IN STNINDEX

L2   QUE ("BLOOD-COAGULATION FACTORS, EPI (EXTRINSIC PATHWAY INHIBITOR)"/BI OR
         "BLOOD-COAGULATION FACTORS, LACI"/BI OR "BLOOD-COAGULATION FACTORS, LI
         POPROTEIN-ASSOCD. COAGULATION INHIBITORS"/BI OR "BLOOD-COAGULATION FAC
         TORS, TFI"/BI OR "EPI BLOOD-COAGULATION FACTORS"/BI OR "EXTRINSIC PATH
         WAY INHIBITOR BLOOD-COAGULATION FACTORS"/BI OR "LACI BLOOD-COAGULATION
          FACTORS"/BI OR "LIPOPROTEIN-ASSOCD. COAGULATION INHIBITOR"/BI OR "LIP
         OPROTEIN-ASSOCD. COAGULATION INHIBITORS BLOOD-COAGULATION FACTORS"/BI
         OR "TISSUE FACTOR INHIBITOR"/BI OR "TISSUE FACTOR PATHWAY INHIBITOR"/B
         I) OR 194554-71-7

=> s chelat? or scaveng? or oxygen displacement gas or antiox?
      7345   FILE ADISCTI
       340   FILE ADISINSIGHT
       295   FILE ADISNEWS
     11761   FILE AGRICOLA
      1773   FILE AQUALINE
      5045   FILE ANABSTR
       525   FILE ANTE
      4366   FILE AQUASCI
      4482   FILE BIOBUSINESS
       140   FILE BIOCOMMERCE
      3132   FILE BIOENG
    107814   FILE BIOSIS
      4238   FILE BIOTECHABS
      4238   FILE BIOTECHDS
     19276   FILE BIOTECHNO
     28342   FILE CABA
     15548   FILE CANCERLIT
    274437   FILE CAPLUS
      2646   FILE CEABA-VTB
       347   FILE CEN
      2574   FILE CIN
      3204   FILE CONFSCI
       453   FILE CROPB
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      1324   FILE CROPU
      7335   FILE DISSABS
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     31592   FILE DDFU
     11108   FILE DGENE
      7719   FILE DRUGB
       400   FILE DRUGMONOG2
       284   FILE IMSDRUGNEWS
     33608   FILE DRUGU
       271   FILE IMSRESEARCH
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     86656   FILE EMBASE
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    42867   FILE ESBIOBASE
     2916   FILE FEDRIP
  37 FILES SEARCHED...
      185   FILE FOMAD
     3997   FILE FOREGE
    16477   FILE FROSTI
    13091   FILE FSTA
     4752   FILE GENBANK
      656   FILE HEALSAFE
    34023   FILE IFIPAT
      275   FILE IMSPRODUCT
    19690   FILE JICST-EPLUS
     1150   FILE KOSMET
    19649   FILE LIFESCI
      174   FILE MEDICONF
    96687   FILE MEDLINE
     2946   FILE NIOSHTIC
     4817   FILE NTIS
      434   FILE NUTRACEUT
     1724   FILE OCEAN
    64775   FILE PASCAL
      336   FILE PHAR
      131   FILE PHARMAML
  58 FILES SEARCHED...
        2   FILE PHIC
      677   FILE PHIN
    16544   FILE PROMT
     1677   FILE PROUSDDR
      718   FILE RDISCLOSURE
   124135   FILE SCISEARCH
       81   FILE SYNTHLINE
   115497   FILE TOXCENTER
   177645   FILE USPATFULL
    10877   FILE USPAT2
      379   FILE VETB
     1202   FILE VETU
     2785   FILE WATER
    62821   FILE WPIDS
      229   FILE WPIFV
  73 FILES SEARCHED...
    62821   FILE WPINDEX

  73 FILES HAVE ONE OR MORE ANSWERS,   74 FILES SEARCHED IN STNINDEX

L3   QUE CHELAT? OR SCAVENG? OR OXYGEN DISPLACEMENT GAS OR ANTIOX?

=> s l2 and l3
   3 FILES SEARCHED...
   6 FILES SEARCHED...
        5   FILE BIOSIS
  12 FILES SEARCHED...
        3   FILE BIOTECHNO
  15 FILES SEARCHED...
        2   FILE CANCERLIT
  17 FILES SEARCHED...
       20   FILE CAPLUS
  20 FILES SEARCHED...
  23 FILES SEARCHED...
        1   FILE DISSABS
  25 FILES SEARCHED...
        1   FILE DDFU
  27 FILES SEARCHED...
  28 FILES SEARCHED...
  30 FILES SEARCHED...
        2   FILE DRUGU
  32 FILES SEARCHED...
  34 FILES SEARCHED...
       17   FILE EMBASE
  35 FILES SEARCHED...
        1   FILE ESBIOBASE
  36 FILES SEARCHED...
  39 FILES SEARCHED...
        9   FILE IFIPAT
  44 FILES SEARCHED...
        1   FILE JICST-EPLUS
  47 FILES SEARCHED...
  49 FILES SEARCHED...
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          8   FILE MEDLINE
  51 FILES SEARCHED...
  54 FILES SEARCHED...
          3   FILE PASCAL
  55 FILES SEARCHED...
  61 FILES SEARCHED...
          8   FILE SCISEARCH
  64 FILES SEARCHED...
          3   FILE TOXCENTER
        383   FILE USPATFULL
  67 FILES SEARCHED...
         25   FILE USPAT2
  69 FILES SEARCHED...
  71 FILES SEARCHED...
          7   FILE WPIDS
  73 FILES SEARCHED...
          7   FILE WPINDEX

  19 FILES HAVE ONE OR MORE ANSWERS,   74 FILES SEARCHED IN STNINDEX

L4   QUE L2 AND L3

=> d rank
F1          383   USPATFULL
F2           25   USPAT2
F3           20   CAPLUS
F4           17   EMBASE
F5            9   IFIPAT
F6            8   MEDLINE
F7            8   SCISEARCH
F8            7   WPIDS
F9            7   WPINDEX
F10           5   BIOSIS
F11           3   BIOTECHNO
F12           3   PASCAL
F13           3   TOXCENTER
F14           2   CANCERLIT
F15           2   DRUGU
F16           1   DISSABS
F17           1   DDFU
F18           1   ESBIOBASE
F19           1   JICST-EPLUS


=> file f4-19
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   22.80      30.77

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=> s l4
   1 FILES SEARCHED...
   3 FILES SEARCHED...
   5 FILES SEARCHED...
   7 FILES SEARCHED...
   8 FILES SEARCHED...
  10 FILES SEARCHED...
  11 FILES SEARCHED...
  13 FILES SEARCHED...
L5          70 L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           43 DUP REM L5 (27 DUPLICATES REMOVED)
                ANSWERS '1-17' FROM FILE EMBASE
                ANSWERS '18-26' FROM FILE IFIPAT
                ANSWERS '27-29' FROM FILE MEDLINE
                ANSWERS '30-32' FROM FILE SCISEARCH
                ANSWERS '33-39' FROM FILE WPIDS
                ANSWER '40' FROM FILE PASCAL
                ANSWER '41' FROM FILE DRUGU
                ANSWER '42' FROM FILE DISSABS
                ANSWER '43' FROM FILE JICST-EPLUS

=> l6 and py<2003
L6 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l6 and py<2003
   3 FILES SEARCHED...
   5 FILES SEARCHED...
   8 FILES SEARCHED...
  11 FILES SEARCHED...
  13 FILES SEARCHED...
L7          27 L6 AND PY<2003

=> d bib abs hit 1-27

L7   ANSWER 1 OF 27  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
AN   2002020984  EMBASE
TI   Clinical developments for treating ARDS.
AU   Eaton S.; Martin G.
CS   G. Martin, Div. of Pulmonary/Critical Care Med., Emory University, 550
     Peachtree Street, NE, Atlanta, GA 30308, United States
SO   Expert Opinion on Investigational Drugs, (2002) 11/1 (37-48).
     Refs: 109
     ISSN: 1354-3784  CODEN: EOIDER
CY   United Kingdom
DT   Journal; General Review
FS   006     Internal Medicine
     014     Radiology
     015     Chest Diseases, Thoracic Surgery and Tuberculosis
     030     Pharmacology
     037     Drug Literature Index
     039     Pharmacy
```

LA English
SL English
AB Acute respiratory distress syndrome (ARDS), is characterised by capillary permeability and pulmonary oedema formation and may complicate a variety of medical and surgical illnesses. As a self-perpetuating state of inflammatory derangement, acute lung injury (ALI)/ARDS is manifest clinically as rapid development of radiographic infiltrates, severe hypoxaemia and reduced lung compliance. Over the years, researchers have made significant progress in elucidating the pathophysiology of this complex syndrome. Therapies targeting specific pathophysiologic steps in the development or persistence of this syndrome are in various stages of laboratory and clinical testing. Results to date have shown nitric oxide (NO) to improve oxygenation in the majority of patients but fail to improve mortality. Surfactant replacement has had limited success in adults, but new formulations and delivery methods may prove beneficial. Several inflammatory mediator-targeted therapies have progressed successfully through early clinical evaluation. Among these, neutrophil elastase inhibitors have shown the most promise and are currently undergoing Phase III trials. Other mediator-targeted therapies, such as prostaglandin E1, IL-10 and platelet activating factor antagonists, have not been found efficacious in large clinical trials of ARDS. However, these therapies, along with coagulation modulators, may have a favourable impact on ARDS by improving outcomes in sepsis, the greatest risk factor for developing this condition. In the interim, supportive care through improvements in mechanical ventilation are beneficial, while specific fluid balance and nutrition strategies may prove advantageous.
SO Expert Opinion on Investigational Drugs, (2002) 11/1 (37-48).
Refs: 109
ISSN: 1354-3784 CODEN: EOIDER
CT Medical Descriptors:
*adult respiratory distress syndrome: CO, complication
*adult respiratory distress syndrome: DI, diagnosis
*adult respiratory distress syndrome: DT, drug therapy
*adult respiratory distress syndrome: ET, etiology
*adult respiratory distress syndrome: TH, therapy
capillary permeability
lung edema
inflammatory disease
lung injury
lung infiltrate
thorax radiography
hypoxemia
disease severity
lung compliance
clinical research
pathophysiology
drug targeting
pathogenesis
clinical laboratory
oxygenation
mortality
substitution therapy
treatment outcome
drug formulation
drug delivery system
drug efficacy
sepsis: DT, drug therapy
risk factor
artificial ventilation
fluid balance
nutrition
human
nonhuman
rat
animal experiment
animal model
controlled study
review
Drug Descriptors:
leukocyte elastase inhibitor: DT, drug therapy
leukocyte elastase inhibitor: PR, pharmaceutics
leukocyte elastase inhibitor: PD, pharmacology
prostaglandin E1: DT, drug therapy
prostaglandin E1: EC, endogenous compound
interleukin 10: DT, drug therapy
interleukin 10: EC, endogenous compound
thrombocyte activating factor antagonist: DT, drug therapy

thrombocyte activating factor antagonist: PR, pharmaceutics
thrombocyte activating factor antagonist: PD, pharmacology
thrombocyte activating factor: EC, endogenous compound
blood clotting factor: EC, endogenous compound
lung surfactant: DV, drug development
lung surfactant: DT, drug therapy
lung surfactant: PR, pharmaceutics
lung surfactant: IH, inhalational drug administration
lung surfactant: TR, intratracheal drug administration
artificial lung surfactant: DV, drug development
artificial lung surfactant: DT, drug therapy
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artificial lung surfactant: IH, inhalational drug administration
artificial lung surfactant: TR, intratracheal drug administration
albumin: DT, drug therapy
furosemide: CM, drug comparison
furosemide: DT, drug therapy
acetylcysteine: DT, drug therapy
thiazolidone: DT, drug therapy
antioxidant: DT, drug therapy
corticosteroid derivative: DT, drug therapy
activated protein C: DT, drug therapy
nitric oxide: CB, drug combination
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nitric oxide: IH, inhalational drug administration
cyclooxygenase 1: EC, endogenous compound
almitrine: CB, drug combination
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almitrine: IV, intravenous drug administration
cyclooxygenase 2: EC, endogenous compound
phenylephrine: CB, drug combination
phenylephrine: DT, drug therapy
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prostacyclin: CB, drug combination
prostacyclin: DT, drug therapy
prostacyclin: IH, inhalational drug administration
poloxomer 188: DT, drug therapy
tissue factor pathway inhibitor: DT, drug therapy
lisofylline: DV, drug development
lisofylline: DT, drug therapy
lisofylline: PD, pharmacology
fluorocarbon: DT, drug therapy
fluorocarbon: IH, inhalational drug administration
fluorocarbon: TR, intratracheal drug administration
perfluorooctyl bromide: DT, drug therapy
perfluorooctyl bromide: PR, pharmaceutics
perfluorooctyl bromide: TR, intratracheal drug administration
prostaglandin synthase inhibitor: DT, drug therapy
prostaglandin synthase inhibitor: PD, pharmacology
prostaglandin synthase inhibitor: IV, intravenous drug administration
ibuprofen: DT, drug therapy
ibuprofen: PD, pharmacology
ibuprofen: IV, intravenous drug administration
atrial natriuretic factor: CB, drug combination
atrial natriuretic factor: CM, drug comparison
atrial natriuretic factor: DT, drug therapy
unindexed drug
unclassified drug
venticute
surfaxin
lung surfactant extract
insasurf

RN (prostaglandin E1) 745-65-3; (thrombocyte activating factor) 64176-80-3, 65154-06-5; (lung surfactant) 99732-49-7; (furosemide) 54-31-9; (acetylcysteine) 616-91-1; (thiazolidone) 28600-65-9; (nitric oxide) 10102-43-9; (almitrine) 27469-53-0; (phenylephrine) 532-38-7, 59-42-7, 61-76-7; (prostacyclin) 35121-78-9, 61849-14-7; (***tissue*** ***factor*** ***pathway*** ***inhibitor***) 116638-34-7; (lisofylline) 100324-81-0, 151852-32-3, 6493-06-7; (fluorocarbon) 11072-16-5; (perfluorooctyl bromide) 423-55-2; (ibuprofen) 15687-27-1; (atrial natriuretic factor) 85637-73-6

L7 ANSWER 2 OF 27 EMBASE
on STN

AN 2001342843 EMBASE
TI The role of high density lipoprotein in sepsis.
AU Van Leeuwen H.J.; Van Beek A.P.; Dallinga-Thie G.M.; Van Strijp J.A.G.; Verhoef J.; Van Kessel K.P.M.
CS H.J. Van Leeuwen, Department of Intensive Care, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, Netherlands. hj.van.leeuwen@rivm.nl
SO Netherlands Journal of Medicine, (2001) 59/3 (102-110).
Refs: 83
ISSN: 0300-2977 CODEN: NJNEEH
PUI S 0300-2977(01)00144-9
CY Netherlands
DT Journal; General Review
FS 024 Anesthesiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SO Netherlands Journal of Medicine, (2001) 59/3 (102-110).
Refs: 83
ISSN: 0300-2977 CODEN: NJNEEH
CT Medical Descriptors:
*sepsis
*lipoprotein metabolism
septic shock
protein protein interaction
immunity
cholesterol transport
lipid transport
liver clearance
detoxification
multiple organ failure
mortality
protein lipid interaction
human
nonhuman
review
Drug Descriptors:
*high density lipoprotein: EC, endogenous compound
*high density lipoprotein: PD, pharmacology
*high density lipoprotein: IV, intravenous drug administration
serum amyloid A: EC, endogenous compound
chylomicron: EC, endogenous compound
chylomicron: PD, pharmacology
chylomicron: IV, intravenous drug administration
apoprotein: EC, endogenous compound
intermediate density lipoprotein: EC, endogenous compound
apolipoprotein A: EC, endogenous compound
cholesterol ester transfer protein: EC, endogenous compound
phospholipid transfer protein: EC, endogenous compound
phosphatidylcholine sterol acyltransferase: EC, endogenous compound
lipopolysaccharide binding protein: EC, endogenous compound
1 alkyl 2 acetylglycerophosphocholine esterase: EC, endogenous compound
tissue factor pathway inhibitor: EC, endogenous compound
clusterin: EC, endogenous compound
triacylglycerol: EC, endogenous compound
cholesterol ester: EC, endogenous compound
CD14 antigen: EC, endogenous compound
glycosylphosphatidylinositol: EC, endogenous compound
interleukin 1: EC, endogenous compound
interleukin 6: EC, endogenous compound
tumor necrosis factor alpha: EC, endogenous compound
C reactive protein: EC, endogenous compound
scavenger receptor: EC, endogenous compound
cholesterol esterase: EC, endogenous compound
G protein coupled receptor: EC, endogenous compound
lipopolysaccharide: EC, endogenous compound
RANTES: EC, endogenous compound
chemotactic factor: EC, endogenous compound
endotoxin
unindexed drug
RN (phosphatidylcholine sterol acyltransferase) 9031-14-5; (lipopolysaccharide binding protein) 203946-66-1; (***tissue*** ***factor*** ***pathway*** ***inhibitor***) 116638-34-7; (C reactive protein) 9007-41-4; (cholesterol esterase) 9026-00-0

L7 ANSWER 3 OF 27 EMBASE

on STN
AN 2001272597 EMBASE
TI Hypolipidaemic and antiplatelet agents.
AU Chilmonczyk Z.; Siluk D.; Kaliszan R.
CS Z. Chilmonczyk, Drug Institute, Chelmska 30/34, 00-725 Warsaw, Poland
SO Expert Opinion on Therapeutic Patents, (2001) 11/8 (1301-1327).
Refs: 100
ISSN: 1354-3776 CODEN: EOTPEG
CY United Kingdom
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LA English
SL English
AB The recent progress of antihyperlipidaemic and antiplatelet drugs widely used in the therapy of cardiovascular disease is reviewed. According to the claimed mechanisms of action, new hypolipidaemic agents originate from groups of compounds such as cholesterol biosynthesis inhibitors, ACAT inhibitors, low density lipoprotein (LDL) uptake promoters, taurocholate receptor antagonists, aP2 inhibitors, PPAR activators and ***antioxidants*** . Since atherosclerosis pathogenesis is a complicated process, coexisting with such disorders as hyperlipidaemia, obesity and insulin resistance syndrome, the majority of compounds do not have clearly defined molecular targets for the treatment of the above complex disorders. Blood platelets play a pivotal role in the development of atherosclerosis and fatal thrombus formation in the course of coronary heart disease. Therefore, there is a great necessity to develop drugs that inhibit platelet aggregation and clot generation. Recently issued patents concern original groups of agents such as fibrinogen and vitronectin receptor inhibitors, drugs targeting thrombin and Factor Xa generation as well as calmodulin modulators. The most promising and most intensively studied are non-peptide and peptide thrombin inhibitors, Factor Xa inhibitors and fibrinogen receptor antagonists. For the better efficacy of platelet anti-aggregatory and antithrombotic treatment new combination therapies are proposed. New approaches to the phenomenon of thrombus formation and combined antithrombotic therapy are claimed to help to reduce fatal events and to decrease adverse effects of cardiovascular disease.
SO Expert Opinion on Therapeutic Patents, (2001) 11/8 (1301-1327).
Refs: 100
ISSN: 1354-3776 CODEN: EOTPEG
AB The recent progress of antihyperlipidaemic and antiplatelet drugs widely used in the therapy of cardiovascular disease is reviewed. According to the claimed mechanisms of action, new hypolipidaemic agents originate from groups of compounds such as cholesterol biosynthesis inhibitors, ACAT inhibitors, low density lipoprotein (LDL) uptake promoters, taurocholate receptor antagonists, aP2 inhibitors, PPAR activators and ***antioxidants*** . Since atherosclerosis pathogenesis is a complicated process, coexisting with such disorders as hyperlipidaemia, obesity and insulin resistance syndrome, the majority of compounds do not have clearly defined molecular targets for the treatment of the above complex disorders. Blood platelets play a pivotal role in the development of atherosclerosis and fatal thrombus formation in the course of coronary heart disease. Therefore, there is a great necessity to develop drugs that inhibit platelet aggregation and clot generation. Recently issued patents concern original groups of agents such as fibrinogen and vitronectin receptor inhibitors, drugs targeting thrombin and Factor Xa generation as well as calmodulin modulators. The most promising and most intensively studied are non-peptide and peptide thrombin inhibitors, Factor Xa inhibitors and fibrinogen receptor antagonists. For the better efficacy of platelet anti-aggregatory and antithrombotic treatment new combination therapies are proposed. New approaches to the phenomenon of thrombus formation and combined antithrombotic therapy are claimed to help to reduce fatal events and to decrease adverse effects of cardiovascular disease.
CT Medical Descriptors:
*hypolipemia
*cardiovascular disease: DT, drug therapy
*cardiovascular disease: ET, etiology
*cardiovascular disease: PC, prevention
review
drug research
drug mechanism

cholesterol synthesis
cholesterol transport
atherosclerosis: DT, drug therapy
atherosclerosis: ET, etiology
atherosclerosis: PC, prevention
pathogenesis
obesity
insulin resistance
drug targeting
thrombocyte aggregation
ischemic heart disease: DT, drug therapy
ischemic heart disease: ET, etiology
ischemic heart disease: PC, prevention
blood clotting
patent
drug efficacy
drug structure
treatment planning
thrombogenesis
human
nonhuman
male
female
mouse
rat
animal experiment
animal model
controlled study
human cell
Drug Descriptors:
*antilipemic agent: AN, drug analysis
*antilipemic agent: CM, drug comparison
*antilipemic agent: DV, drug development
*antilipemic agent: DT, drug therapy
*antilipemic agent: PD, pharmacology
*antithrombocytic agent: AN, drug analysis
*antithrombocytic agent: CM, drug comparison
*antithrombocytic agent: DV, drug development
*antithrombocytic agent: DT, drug therapy
*antithrombocytic agent: PD, pharmacology
cholesterol: EC, endogenous compound
cholesterol acyltransferase: EC, endogenous compound
cholesterol acyltransferase inhibitor: AN, drug analysis
cholesterol acyltransferase inhibitor: CM, drug comparison
cholesterol acyltransferase inhibitor: DV, drug development
cholesterol acyltransferase inhibitor: DT, drug therapy
cholesterol acyltransferase inhibitor: PD, pharmacology
low density lipoprotein: EC, endogenous compound
taurocholic acid: EC, endogenous compound
peroxisome proliferator activated receptor: EC, endogenous compound
peroxisome proliferator activated receptor agonist: AN, drug analysis
peroxisome proliferator activated receptor agonist: CM, drug comparison
peroxisome proliferator activated receptor agonist: DV, drug development
peroxisome proliferator activated receptor agonist: DT, drug therapy
peroxisome proliferator activated receptor agonist: PD, pharmacology
antioxidant: AN, drug analysis
antioxidant: CM, drug comparison
antioxidant: DV, drug development
antioxidant: DT, drug therapy
antioxidant: PD, pharmacology
lipoprotein A: EC, endogenous compound
tissue factor pathway inhibitor: AN, drug analysis
tissue factor pathway inhibitor: CM, drug comparison
tissue factor pathway inhibitor: DV, drug development
tissue factor pathway inhibitor: DT, drug therapy
tissue factor pathway inhibitor: PD, pharmacology
fibrinogen: EC, endogenous compound
fibrinogen receptor: EC, endogenous compound
fibrinogen receptor antagonist: AN, drug analysis
fibrinogen receptor antagonist: CM, drug comparison
fibrinogen receptor antagonist: DV, drug development
fibrinogen receptor antagonist: DT, drug therapy
fibrinogen receptor antagonist: PD, pharmacology
vitronectin: EC, endogenous compound
vitronectin receptor: EC, endogenous compound
thrombin: EC, endogenous compound
blood clotting factor 10a: EC, endogenous compound

calmodulin: EC, endogenous compound
calmodulin inhibitor: AN, drug analysis
calmodulin inhibitor: CM, drug comparison
calmodulin inhibitor: DV, drug development
calmodulin inhibitor: DT, drug therapy
calmodulin inhibitor: PD, pharmacology
thrombin inhibitor: AN, drug analysis
thrombin inhibitor: CM, drug comparison
thrombin inhibitor: DV, drug development
thrombin inhibitor: DT, drug therapy
thrombin inhibitor: PD, pharmacology
peptide derivative: AN, drug analysis
peptide derivative: CM, drug comparison
peptide derivative: DV, drug development
peptide derivative: DT, drug therapy
peptide derivative: PD, pharmacology
omeprazole: AN, drug analysis
omeprazole: CM, drug comparison
omeprazole: DV, drug development
omeprazole: DT, drug therapy
omeprazole: PD, pharmacology
simvastatin: AN, drug analysis
simvastatin: CM, drug comparison
simvastatin: DV, drug development
simvastatin: DT, drug therapy
simvastatin: PD, pharmacology
atorvastatin: AN, drug analysis
atorvastatin: CM, drug comparison
atorvastatin: DV, drug development
atorvastatin: DT, drug therapy
atorvastatin: PD, pharmacology
ticlopidine: AN, drug analysis
ticlopidine: CM, drug comparison
ticlopidine: DV, drug development
ticlopidine: DT, drug therapy
ticlopidine: PD, pharmacology
clopidogrel: AN, drug analysis
clopidogrel: CM, drug comparison
clopidogrel: DV, drug development
clopidogrel: DT, drug therapy
clopidogrel: PD, pharmacology
membrane protein: EC, endogenous compound
unindexed drug

RN (cholesterol) 57-88-5; (cholesterol acyltransferase) 9027-63-8; (taurocholic acid) 145-42-6, 59005-70-8, 81-24-3; (***tissue*** ***factor*** ***pathway*** ***inhibitor***) 116638-34-7; (fibrinogen) 9001-32-5; (thrombin) 9002-04-4; (blood clotting factor 10a) 72162-96-0, 9002-05-5; (omeprazole) 73590-58-6, 95510-70-6; (simvastatin) 79902-63-9; (atorvastatin) 134523-00-5, 134523-03-8; (ticlopidine) 53885-35-1, 55142-85-3; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8

L7 ANSWER 4 OF 27 EMBASE
on STN

AN 2001262804 EMBASE

TI Hepatic response to sepsis: Interaction between coagulation and inflammatory processes.

AU Dhainaut J.-F.; Marin N.; Mignon A.; Vinsonneau C.; Sprung C.

CS Dr. J.-F. Dhainaut, Medical Intensive Care Unit, Cochin Port-Royal Univ.-Hospital, Paris V University, Paris, France

SO Critical Care Medicine, (2001) 29/7 SUPPL. (S42-S47).
Refs: 63
ISSN: 0090-3493 CODEN: CCMDC7

CY United States

DT Journal; Conference Article

FS 005 General Pathology and Pathological Anatomy
024 Anesthesiology
025 Hematology
026 Immunology, Serology and Transplantation
048 Gastroenterology

LA English

SL English

AB Objectives: a) To review the hepatic response to sepsis and to establish how this response contributes to coagulation and inflammatory processes; b) to review the physiologic and biochemical mechanisms that suggest hepatic dysfunction may occur during sepsis, enhance procoagulant and proinflammatory activities, and participate in the potential evolution to

multiple organ dysfunction syndrome. Data Sources: A summary of published medical literature from MEDLINE search files and published reviews on liver function in experimental and human sepsis. Data Summary: In sepsis, the liver plays a major role in host defense mechanisms. Kupffer cells are responsible for bacterial ***scavenging*** , bacterial products inactivation, and inflammatory mediators clearance and production. Hepatocytes, via receptors for many proinflammatory cytokines, modify their metabolic pathway toward gluconeogenesis, amino-acid uptake, and increased synthesis of coagulant and complement factors and protease inhibitors. The acute-phase protein (APP) response also contributes to the procoagulant state, especially by enhancing the inhibition of protein C (.alpha.(1)-antitrypsin and .alpha.(2)-macroglobulin) and by decreasing liver synthesis of protein C and antithrombin (negative APPs). Elevated C-reactive protein levels (positive APPs) promote the expression of tissue factor by mononuclear cells. Increased liver production of thrombin-activatable fibrinolytic inhibitor (positive APPs) enhances fibrinolysis inhibition. Conversely, such hepatic inflammatory and coagulation processes in sepsis may alter the function of this organ. Indeed, the liver can be injured by activated Kupffer cells that release chemokines, attract blood neutrophils into the liver, and activate them. Neutrophils upregulate their surface adhesion molecules, tissue factor, and Kupffer cells, whereas ***tissue*** ***factor*** ***pathway*** ***inhibitor*** and thrombomodulin are almost undetectable in endothelial cells. This may lead to microcirculatory disturbances, fibrin deposition, hepatocyte injury, endotoxin and bacteria spillover, and multiple organ failure. Conclusions: In sepsis, the liver participates in host defense and tissue repair through hepatic cell cross-talk that controls most of the coagulation and inflammatory processes. When this control is not adequate, a secondary hepatic dysfunction may occur and may sometimes lead to bacterial products spillover, enhanced procoagulant and inflammatory processes, and in turn, multiple organ failure and death.

SO Critical Care Medicine, (2001) 29/7 SUPPL. (S42-S47).
Refs: 63
ISSN: 0090-3493 CODEN: CCMDC7

AB Objectives: a) To review the hepatic response to sepsis and to establish how this response contributes to coagulation and inflammatory processes; b) to review the physiologic and biochemical mechanisms that suggest hepatic dysfunction may occur during sepsis, enhance procoagulant and proinflammatory activities, and participate in the potential evolution to multiple organ dysfunction syndrome. Data Sources: A summary of published medical literature from MEDLINE search files and published reviews on liver function in experimental and human sepsis. Data Summary: In sepsis, the liver plays a major role in host defense mechanisms. Kupffer cells are responsible for bacterial ***scavenging*** , bacterial products inactivation, and inflammatory mediators clearance and production. Hepatocytes, via receptors for many proinflammatory cytokines, modify their metabolic pathway toward gluconeogenesis, amino-acid uptake, and increased synthesis of coagulant and complement factors and protease inhibitors. The acute-phase protein (APP) response also contributes to the procoagulant state, especially by enhancing the inhibition of protein C (.alpha.(1)-antitrypsin and .alpha.(2)-macroglobulin) and by decreasing liver synthesis of protein C and antithrombin (negative APPs). Elevated C-reactive protein levels (positive APPs) promote the expression of tissue factor by mononuclear cells. Increased liver production of thrombin-activatable fibrinolytic inhibitor (positive APPs) enhances fibrinolysis inhibition. Conversely, such hepatic inflammatory and coagulation processes in sepsis may alter the function of this organ. Indeed, the liver can be injured by activated Kupffer cells that release chemokines, attract blood neutrophils into the liver, and activate them. Neutrophils upregulate their surface adhesion molecules, tissue factor, and Kupffer cells, whereas ***tissue*** ***factor*** ***pathway*** ***inhibitor*** and thrombomodulin are almost undetectable in endothelial cells. This may lead to microcirculatory disturbances, fibrin deposition, hepatocyte injury, endotoxin and bacteria spillover, and multiple organ failure. Conclusions: In sepsis, the liver participates in host defense and tissue repair through hepatic cell cross-talk that controls most of the coagulation and inflammatory processes. When this control is not adequate, a secondary hepatic dysfunction may occur and may sometimes lead to bacterial products spillover, enhanced procoagulant and inflammatory processes, and in turn, multiple organ failure and death.

CT Medical Descriptors:
*sepsis
*liver function
*blood clotting
*inflammation

liver dysfunction
multiple organ failure
medical information
host resistance
Kupffer cell
scavenging system
gluconeogenesis
amino acid transport
complement factor
protein synthesis
mononuclear cell
neutrophil
fibrin deposition
liver cell damage
signal transduction
tissue repair
immunity
human
controlled study
human cell
conference paper
priority journal
Drug Descriptors:
cytokine: EC, endogenous compound
proteinase inhibitor
acute phase protein: EC, endogenous compound
protein C: EC, endogenous compound
alpha 1 antitrypsin: EC, endogenous compound
alpha 2 macroglobulin: EC, endogenous compound
C reactive protein: EC, endogenous compound
thrombin: EC, endogenous compound
antifibrinolytic agent
chemokine: EC, endogenous compound
thromboplastin: EC, endogenous compound

L7 ANSWER 5 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2001112156 EMBASE
TI Tissue factor as a therapeutic target.
AU Key N.S.; Bach R.R.
CS Dr. N.S. Key, Div. of Hematol. Oncol./Transplant., University of Minnesota, Medical School, Minneapolis, MN 55455, United States.
keyxx001@tc.umn.edu
SO Thrombosis and Haemostasis, (2001) 85/3 (375-376).
Refs: 10
ISSN: 0340-6245 CODEN: THHADQ
CY Germany
DT Journal; Note
FS 025 Hematology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
030 Pharmacology
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
016 Cancer
LA English
SO Thrombosis and Haemostasis, (2001) 85/3 (375-376).
Refs: 10
ISSN: 0340-6245 CODEN: THHADQ
CT Medical Descriptors:
human
clinical trial
nonhuman
drug targeting
blood clotting
protein degradation
in vivo study
disseminated intravascular clotting
heart infarction: DT, drug therapy
atherosclerotic plaque
unstable angina pectoris: DT, drug therapy
artery thrombosis: ET, etiology
artery intima proliferation: ET, etiology
tumor cell line
angiogenesis
protein expression
disease model

genetic transcription
genetic regulation
antiinflammatory activity
antioxidant activity
drug inhibition
drug potency
drug protein binding
antibody affinity
fibrin formation
drug design
sepsis: DT, drug therapy
cancer: DT, drug therapy
note
priority journal
Drug Descriptors:
*thromboplastin: EC, endogenous compound
cytokine receptor: EC, endogenous compound
blood clotting factor 7: EC, endogenous compound
blood clotting factor 8a: EC, endogenous compound
enzyme precursor: EC, endogenous compound
blood clotting factor 9: EC, endogenous compound
blood clotting factor 10: EC, endogenous compound
curcumin: PD, pharmacology
curcumin: DT, drug therapy
curcumin: DV, drug development
curcumin: CT, clinical trial
thrombocyte antibody: PD, pharmacology
thrombocyte antibody: DT, drug therapy
thrombocyte antibody: DV, drug development
thrombocyte antibody: CT, clinical trial
proteinase inhibitor: PD, pharmacology
proteinase inhibitor: DT, drug therapy
proteinase inhibitor: DV, drug development
proteinase inhibitor: CT, clinical trial
recombinant tissue factor pathway inhibitor: PD, pharmacology
recombinant tissue factor pathway inhibitor: DT, drug therapy
recombinant tissue factor pathway inhibitor: DV, drug development
recombinant tissue factor pathway inhibitor: CT, clinical trial
anticoagulant agent: PD, pharmacology
anticoagulant agent: DT, drug therapy
anticoagulant agent: DV, drug development
anticoagulant agent: CT, clinical trial
anticoagulant protein: EC, endogenous compound
human monoclonal antibody: PD, pharmacology
human monoclonal antibody: DT, drug therapy
human monoclonal antibody: DV, drug development
human monoclonal antibody: CT, clinical trial
chimeric protein: EC, endogenous compound
phosphatidylserine: EC, endogenous compound
lipocortin 5: PD, pharmacology
lipocortin 5: DT, drug therapy
lipocortin 5: DV, drug development
lipocortin 5: CT, clinical trial

L7 ANSWER 6 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2000236183 EMBASE
TI Gene therapy for atherosclerossis and restenosis.
AU Kivela A.; Turunen A.-M.; Yla-Herttuala S.
CS S. Yla-Herttuala, Al Virtanen Institute, University of Kuopio, PO Box 1627, 70211 Kuopio, Finland. seppo.ylaherttuala@uku.fi
SO Current Opinion in Cardiovascular, Pulmonary and Renal Investigational Drugs, (2000) 2/3 (244-249).
Refs: 66
ISSN: 1464-8482 CODEN: CCPRFX
CY United Kingdom
DT Journal; General Review
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LA English
SO Current Opinion in Cardiovascular, Pulmonary and Renal Investigational Drugs, (2000) 2/3 (244-249).
Refs: 66
ISSN: 1464-8482 CODEN: CCPRFX
CT Medical Descriptors:

*atherosclerosis: TH, therapy
*atherosclerosis: DT, drug therapy
*restenosis: TH, therapy
*restenosis: PC, prevention
*restenosis: DT, drug therapy
human
clinical trial
nonhuman
gene therapy
angiogenesis
hypercholesterolemia: TH, therapy
virus vector
gene targeting
coronary artery disease: SU, surgery
coronary artery bypass surgery
transluminal coronary angioplasty
gene transfer
thrombosis prevention
drug inhibition
cell proliferation
Adenovirus
Retrovirus
Lentivirinae
Adeno associated virus
Herpes virus
Epstein Barr virus
DNA transfection
drug delivery system
review
Drug Descriptors:
low density lipoprotein: EC, endogenous compound
low density lipoprotein receptor: DT, drug therapy
high density lipoprotein: EC, endogenous compound
apolipoprotein A1: EC, endogenous compound
very low density lipoprotein: EC, endogenous compound
chylomicron: EC, endogenous compound
lipoprotein A: CB, drug combination
lipoprotein A: PD, pharmacology
lipoprotein A: DT, drug therapy
apolipoprotein A: CB, drug combination
apolipoprotein A: PD, pharmacology
apolipoprotein A: DT, drug therapy
plasminogen: EC, endogenous compound
fibrin: EC, endogenous compound
scavenger receptor: PD, pharmacology
tissue plasminogen activator: DT, drug therapy
recombinant hirudin: DT, drug therapy
tissue factor pathway inhibitor: DT, drug therapy
platelet derived growth factor: EC, endogenous compound
vasculotropin: DT, drug therapy
matrix metalloproteinase: EC, endogenous compound
tissue inhibitor of metalloproteinase 1: DT, drug therapy
nitric oxide: DT, drug therapy
antisense oligonucleotide: CT, clinical trial
antisense oligonucleotide: DT, drug therapy
acidic fibroblast growth factor: DT, drug therapy
basic fibroblast growth factor: DT, drug therapy
liposome: DT, drug therapy
polymer: DT, drug therapy
plasmid DNA: IM, intramuscular drug administration
plasmid DNA: DT, drug therapy
apolipoprotein E: DT, drug therapy
apolipoprotein E: PD, pharmacology
lipofectin
RN (plasminogen) 9001-91-6; (fibrin) 9001-31-4; (tissue plasminogen activator) 105913-11-9; (***tissue*** ***factor*** ***pathway*** ***inhibitor***) 116638-34-7; (vasculotropin) 127464-60-2; (tissue inhibitor of metalloproteinase 1) 140208-24-8; (nitric oxide) 10102-43-9; (acidic fibroblast growth factor) 106096-92-8; (basic fibroblast growth factor) 106096-93-9; (lipofectin) 128835-92-7

L7 ANSWER 7 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2000139642 EMBASE
TI Endothelial function and hemostasis.
AU Becker B.F.; Heindl B.; Kupatt C.; Zahler S.
CS Dr. B.F. Becker, Dept. of Physiology, University of Munich, Pettenkofer

Str. 12, D-80336 Munich, Germany
SO Zeitschrift fur Kardiologie, (2000) 89/3 (160-167).
Refs: 54
ISSN: 0300-5860 CODEN: ZKRDAX
CY Germany
DT Journal; Conference Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
LA English
SL English
AB The vascular endothelium influences not only the three classically interacting components of hemostasis: the vessel, the blood platelets and the clotting and fibrinolytic systems of plasma, but also the natural sequelae: inflammation and tissue repair. Two principal modes of endothelial behaviour may be differentiated, best defined as an anti- and a prothrombotic state. Under physiological conditions endothelium mediates vascular dilatation (formation of NO, PGI2, adenosine, hyperpolarising factor), prevents platelet adhesion and activation (production of adenosine, NO and PGI2, removal of ADP), blocks thrombin formation (***tissue*** ***factor*** ***pathway*** ***inhibitor*** , activation of protein C via thrombomodulin, activation of antithrombin III) and mitigates fibrin deposition (t- and scuplasminogen activator production). Adhesion and transmigration of inflammatory leukocytes are attenuated, e.g. by NO and IL-10, and oxygen radicals are efficiently ***scavenged*** (urate, NO, glutathione, SOD). When the endothelium is physically disrupted or functionally perturbed by postischemic reperfusion, acute and chronic inflammation, atherosclerosis, diabetes and chronic arterial hypertension, then completely opposing actions pertain. This prothrombotic, proinflammatory state is characterised by vasoconstriction, platelet and leukocyte activation and adhesion (externalisation, expression and upregulation of von Willebrand factor, platelet activating factor, P-selectin, ICAM-1, IL-8, MCP-1, TNFa, etc.), promotion of thrombin formation, coagulation and fibrin deposition at the vascular wall (expression of tissue factor, PAI-1, phosphatidyl serine, etc.) and, in platelet-leukocyte coaggregates, additional inflammatory interactions via attachment of platelet CD40-ligand to endothelial, monocyte and B-cell CD40. Since thrombin formation and inflammatory stimulation set the stage for later tissue repair, complete abolition of such endothelial responses cannot be the goal of clinical interventions aimed at limiting procoagulatory, prothrombotic actions of a dysfunctional vascular endothelium.
SO Zeitschrift fur Kardiologie, (2000) 89/3 (160-167).
Refs: 54
ISSN: 0300-5860 CODEN: ZKRDAX
AB The vascular endothelium influences not only the three classically interacting components of hemostasis: the vessel, the blood platelets and the clotting and fibrinolytic systems of plasma, but also the natural sequelae: inflammation and tissue repair. Two principal modes of endothelial behaviour may be differentiated, best defined as an anti- and a prothrombotic state. Under physiological conditions endothelium mediates vascular dilatation (formation of NO, PGI2, adenosine, hyperpolarising factor), prevents platelet adhesion and activation (production of adenosine, NO and PGI2, removal of ADP), blocks thrombin formation (***tissue*** ***factor*** ***pathway*** ***inhibitor*** , activation of protein C via thrombomodulin, activation of antithrombin III) and mitigates fibrin deposition (t- and scuplasminogen activator production). Adhesion and transmigration of inflammatory leukocytes are attenuated, e.g. by NO and IL-10, and oxygen radicals are efficiently ***scavenged*** (urate, NO, glutathione, SOD). When the endothelium is physically disrupted or functionally perturbed by postischemic reperfusion, acute and chronic inflammation, atherosclerosis, diabetes and chronic arterial hypertension, then completely opposing actions pertain. This prothrombotic, proinflammatory state is characterised by vasoconstriction, platelet and leukocyte activation and adhesion (externalisation, expression and upregulation of von Willebrand factor, platelet activating factor, P-selectin, ICAM-1, IL-8, MCP-1, TNFa, etc.), promotion of thrombin formation, coagulation and fibrin deposition at the vascular wall (expression of tissue factor, PAI-1, phosphatidyl serine, etc.) and, in platelet-leukocyte coaggregates, additional inflammatory interactions via attachment of platelet CD40-ligand to endothelial, monocyte and B-cell CD40. Since thrombin formation and inflammatory stimulation set the stage for later tissue repair, complete abolition of such endothelial responses cannot be the goal of clinical interventions aimed at limiting procoagulatory, prothrombotic actions of a dysfunctional vascular endothelium.

L7 ANSWER 8 OF 27 EMBASE

on STN
AN 1999371654 EMBASE
TI Histopathology and pathogenesis of plaque instability and thrombus formation.
AU Zaman A.G.; Helft G.; Osende J.I.; Fuster V.; Badimon J.J.
CS J.J. Badimon, Cardiovasc. Biol. Res. Laboratory, Z./M. A. Wiener Cardiovasc. Inst., Mount Sinai School of Medicine, New York, NY 10029, United States
SO Drugs of Today, (1999) 35/8 (641-656).
Refs: 70
ISSN: 0025-7656 CODEN: MDACAP
CY Spain
DT Journal; General Review
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English
AB Our knowledge of the pathogenesis of plaque instability has undergone profound changes in recent years. Research in this field has been driven by the fact that atherosclerosis and its thrombotic complications continue to be the major cause of mortality and morbidity throughout the industrialized world. The different types of atherosclerotic lesions, mechanisms of atherosclerotic progression, plaque vulnerability and rupture are now better understood. This has led to evolution of therapeutic strategies designed to stabilize atherosclerotic plaque and to reduce progression. Furthermore, knowledge of mechanisms leading to thrombosis after plaque rupture have led to the development of antithrombotic strategies to prevent and reduce complications arising from such an event. This review will describe the histopathology and pathogenesis leading to plaque instability, the factors associated with subsequent rupture and assess the role of thrombosis in the progression of atherosclerotic disease. We will focus on current therapeutic strategies to identify and reduce vulnerable plaques and speculate on future areas for research.
SO Drugs of Today, (1999) 35/8 (641-656).
Refs: 70
ISSN: 0025-7656 CODEN: MDACAP
CT Medical Descriptors:
*atherosclerotic plaque: DT, drug therapy
*atherosclerotic plaque: ET, etiology
*atherosclerotic plaque: PC, prevention
*thrombogenesis
atherosclerosis: DT, drug therapy
atherosclerosis: ET, etiology
atherosclerosis: PC, prevention
disease classification
risk factor
smoking
pathogenesis
histopathology
hormone substitution
human
review
Drug Descriptors:
antilipemic agent: CB, drug combination
antilipemic agent: DT, drug therapy
antilipemic agent: PD, pharmacology
antioxidant: CB, drug combination
antioxidant: DT, drug therapy
alpha tocopherol: DT, drug therapy
gamma tocopherol: DT, drug therapy
tocopherol derivative: DT, drug therapy
ascorbic acid: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
quinapril: DT, drug therapy
estrogen: CB, drug combination
medroxyprogesterone: CB, drug combination
antibiotic agent: DT, drug therapy
macrolide: DT, drug therapy
beta adrenergic receptor blocking agent: DT, drug therapy
anticoagulant agent: DT, drug therapy
heparin: DT, drug therapy
warfarin: DT, drug therapy
low molecular weight heparin: DT, drug therapy
antithrombin: DT, drug therapy
acetylsalicylic acid: DT, drug therapy
ticlopidine: DT, drug therapy

clopidogrel: DT, drug therapy
fibrinogen receptor antagonist: DT, drug therapy
tissue factor pathway inhibitor: DT, drug therapy
blood clotting factor 10a inhibitor: DT, drug therapy
tick anticoagulant peptide: DT, drug therapy
RN (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (gamma tocopherol) 7616-22-0; (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (quinapril) 82586-55-8, 85441-61-8; (medroxyprogesterone) 520-85-4; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (antithrombin) 9000-94-6; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (ticlopidine) 53885-35-1, 55142-85-3; (clopidogrel) 113665-84-2, 120202-66-6, 90055-48-4, 94188-84-8; (***tissue*** ***factor*** ***pathway*** ***inhibitor***) 116638-34-7

L7 ANSWER 9 OF 27 EMBASE
on STN
AN 97054731 EMBASE
DN 1997054731
TI Regulation of tissue factor initiated thrombin generation by the stoichiometric inhibitors ***tissue*** ***factor*** ***pathway*** ***inhibitor*** , antithrombin-III, and heparin cofactor-II.
AU Van't Veer C.; Mann K.G.
CS K.G. Mann, Department of Biochemistry, University of Vermont, Burlington, VT 05405-0068, United States
SO Journal of Biological Chemistry, (1997) 272/7 (4367-4377).
Refs: 44
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB The effects of the stoichiometric inhibitors ***tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI), antithrombin. III (AT-III) and heparin cofactor-II (HC-II) on thrombin generation were evaluated in a reaction system composed of coagulation factors VIIa, X, IX, VIII, and V and prothrombin initiated by tissue factor (TF) and phospholipids. Initiation of the reaction in the absence of inhibitors resulted in explosive thrombin generation for factor VIIa.cntdot.TF concentrations varying from 100 to 0.25 pM with the lag time or initiation phase of thrombin generation increasing from 0 to 180 s with decreasing factor VIIa.cntdot.TF concentrations. During the propagation phase, prothrombin is quantitatively activated to 1.4 .mu.M .alpha.-thrombin. At normal plasma concentration (2.5 .mu.M) full-length recombinant TFPI prolonged the initiation phase of thrombin generation 2-fold, and the rate of thrombin generation in the propagation phase of the reaction was 25-50% that of the uninhibited reaction when the reaction was initiated with 1.25-20 pM factor VIIa.cntdot.TF. Inhibition of the reaction by TFPI is associated with a delay in factor V activation. In the presence of TFPI no explosive thrombin generation was observed when factor VIII was omitted from reactions initiated by factor VIIa.cntdot.TF concentrations .ltoreq.20 pM. This indicates that in the presence of TFPI the factor IXa.cntdot.factor VIIIa pathway becomes essential at low factor VIIa.cntdot.TF concentrations. In the reconstituted system, AT-III (3.4 .mu.M) did not prolong the initiation phase of thrombin generation when the reaction was initiated with 1.25 pM factor VIIa.cntdot.TF, nor did AT-III delay factor V activation. The rate of thrombin formation in the presence of AT-III was reduced to 30% that of the uninhibited reaction, and the .alpha.-thrombin formed was rapidly inhibited subsequent to its generation. The addition of HC-II alone at its physiological concentration (1.38 .mu.M) to the procoagulant mixture did not alter the rate or extent of thrombin generation. Subsequently, the thrombin formed was slowly inhibited by HC-II. The slow inactivation of thrombin by HC-II does not contribute to thrombin inhibition in the presence of AT-III. In contrast, the combination of physiological levels of AT-III and TFPI inhibited explosive thrombin generation initiated by 1.25 pM factor VIIa.cntdot.TF completely. The absence of prothrombin consumption indicated that the combination of TFPI and AT-III is able to pre vent the formation of prothrombinase activity at low factor VIIa. TF concentrations. The data indicate that TFPI potentiates the action of AT-III by decreasing the rate of formation and thus the amount of catalyst formed in the reaction, enabling AT-III to effectively ***scavenge*** the limited traces of factor IXa and factor Xa formed in the presence of TFPI. The initiation of thrombin generation by increasing factor VIIa.cntdot.TF concentrations in

the presence of physiological concentrations of TFPI and AT-III showed dramatic changes in the maximal rates of thrombin generation over small changes in initiator concentration. These data demonstrate that significant thrombin generation becomes a 'threshold-limited' event with regard to the initiating factor VIIa.cntdot.TF concentration in the presence of TFPI and AT-III.

TI Regulation of tissue factor initiated thrombin generation by the stoichiometric inhibitors ***tissue*** ***factor*** ***pathway*** ***inhibitor*** , antithrombin-III, and heparin cofactor-II.

SO Journal of Biological Chemistry, (1997) 272/7 (4367-4377).
Refs: 44
ISSN: 0021-9258 CODEN: JBCHA3

AB The effects of the stoichiometric inhibitors ***tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI), antithrombin. III (AT-III) and heparin cofactor-II (HC-II) on thrombin generation were evaluated in a reaction system composed of coagulation factors VIIa, X, IX, VIII, and V and prothrombin initiated by tissue factor (TF) and phospholipids. Initiation of the reaction in the absence of inhibitors resulted in explosive thrombin generation for factor VIIa.cntdot.TF concentrations varying from 100 to 0.25 pM with the lag time or initiation phase of thrombin generation increasing from 0 to 180 s with decreasing factor VIIa.cntdot.TF concentrations. During the propagation phase, prothrombin is quantitatively activated to 1.4 .mu.M .alpha.-thrombin. At normal plasma concentration (2.5 .mu.M) full-length recombinant TFPI prolonged the initiation phase of thrombin generation 2-fold, and the rate of thrombin generation in the propagation phase of the reaction was 25-50% that of the uninhibited reaction when the reaction was initiated with 1.25-20 pM factor VIIa.cntdot.TF. Inhibition of the reaction by TFPI is associated with a delay in factor V activation. In the presence of TFPI no explosive thrombin generation was observed when factor VIII was omitted from reactions initiated by factor VIIa.cntdot.TF concentrations .ltoreq.20 pM. This indicates that in the presence of TFPI the factor IXa.cntdot.factor VIIIa pathway becomes essential at low factor VIIa.cntdot.TF concentrations. In the reconstituted system, AT-III (3.4 .mu.M) did not prolong the initiation phase of thrombin generation when the reaction was initiated with 1.25 pM factor VIIa.cntdot.TF, nor did AT-III delay factor V activation. The rate of thrombin formation in the presence of AT-III was reduced to 30% that of the uninhibited reaction, and the .alpha.-thrombin formed was rapidly inhibited subsequent to its generation. The addition of HC-II alone at its physiological concentration (1.38 .mu.M) to the procoagulant mixture did not alter the rate or extent of thrombin generation. Subsequently, the thrombin formed was slowly inhibited by HC-II. The slow inactivation of thrombin by HC-II does not contribute to thrombin inhibition in the presence of AT-III. In contrast, the combination of physiological levels of AT-III and TFPI inhibited explosive thrombin generation initiated by 1.25 pM factor VIIa.cntdot.TF completely. The absence of prothrombin consumption indicated that the combination of TFPI and AT-III is able to pre vent the formation of prothrombinase activity at low factor VIIa. TF concentrations. The data indicate that TFPI potentiates the action of AT-III by decreasing the rate of formation and thus the amount of catalyst formed in the reaction, enabling AT-III to effectively ***scavenge*** the limited traces of factor IXa and factor Xa formed in the presence of TFPI. The initiation of thrombin generation by increasing factor VIIa.cntdot.TF concentrations in the presence of physiological concentrations of TFPI and AT-III showed dramatic changes in the maximal rates of thrombin generation over small changes in initiator concentration. These data demonstrate that significant thrombin generation becomes a 'threshold-limited' event with regard to the initiating factor VIIa.cntdot.TF concentration in the presence of TFPI and AT-III.

L7 ANSWER 10 OF 27 EMBASE
on STN

AN 94089427 EMBASE
DN 1994089427
TI Influences of lipid-modifying agents on hemostasis.
AU Sirtori C.R.; Colli S.
CS via Balzaretti 9,20133 Milano, Italy
SO Cardiovascular Drugs and Therapy, (1993) 7/5 (817-823).
ISSN: 0920-3206 CODEN: CDTHET
CY United States
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English

AB Drugs affecting lipid metabolism may influence, to a variable extent, the hemostatic system, that is, platelet activation, fibrinogen, and fibrinolysis. These effects may or may not be linked to the activity of these compounds on the lipid/lipoprotein profile. For this reason it may be important to consider the effects of hypolipidemic drugs on the different aspects of hemostasis, because this may allow a better understanding of their clinical use, as well as, eventually, a more proper selection in individual patients. Among the major lipid-lowering agents, fibric acids belong to a multifaceted series of abnormal fatty acids known to interact with a liver nuclear receptor, in turn activating fatty acid catabolism. A similar activity may be exerted by n-3 fatty acids from fish, as well as by other chemically related or unrelated compounds. Among fibric acids all but gemfibrozil can reduce fibrinogen levels; this last drug can, however, apparently activate fibrinolysis. Among the selective cholesterol-lowering medications, both resins and HMG CoA reductase inhibitors may reduce, in some patients, over prolonged periods of treatment, platelet sensitivity to major aggregants. This effect may be seen best with non-liver-selective agents (e.g., simvastatin), although recent data cast doubt on its constancy. A direct comparative evaluation of different HMG CoA reductase inhibitors on platelet aggregability has never been carried out. These last drugs may also reduce the circulating levels of the ***tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI), transported by LDL in plasma, which is a potentially negative effect. A lipid-lowering molecule with ***antioxidant*** activity, for example, probucol, may also possibly play a role in controlling platelet activation. Probucol was recently shown to reduce the excretion of thromboxane metabolites in patients with homocystinuria. The complex pattern of effects of this molecule may, however, also suggest other mechanisms.

SO Cardiovascular Drugs and Therapy, (1993) 7/5 (817-823).
ISSN: 0920-3206 CODEN: CDTHET

AB Drugs affecting lipid metabolism may influence, to a variable extent, the hemostatic system, that is, platelet activation, fibrinogen, and fibrinolysis. These effects may or may not be linked to the activity of these compounds on the lipid/lipoprotein profile. For this reason it may be important to consider the effects of hypolipidemic drugs on the different aspects of hemostasis, because this may allow a better understanding of their clinical use, as well as, eventually, a more proper selection in individual patients. Among the major lipid-lowering agents, fibric acids belong to a multifaceted series of abnormal fatty acids known to interact with a liver nuclear receptor, in turn activating fatty acid catabolism. A similar activity may be exerted by n-3 fatty acids from fish, as well as by other chemically related or unrelated compounds. Among fibric acids all but gemfibrozil can reduce fibrinogen levels; this last drug can, however, apparently activate fibrinolysis. Among the selective cholesterol-lowering medications, both resins and HMG CoA reductase inhibitors may reduce, in some patients, over prolonged periods of treatment, platelet sensitivity to major aggregants. This effect may be seen best with non-liver-selective agents (e.g., simvastatin), although recent data cast doubt on its constancy. A direct comparative evaluation of different HMG CoA reductase inhibitors on platelet aggregability has never been carried out. These last drugs may also reduce the circulating levels of the ***tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI), transported by LDL in plasma, which is a potentially negative effect. A lipid-lowering molecule with ***antioxidant*** activity, for example, probucol, may also possibly play a role in controlling platelet activation. Probucol was recently shown to reduce the excretion of thromboxane metabolites in patients with homocystinuria. The complex pattern of effects of this molecule may, however, also suggest other mechanisms.

L7 ANSWER 11 OF 27 EMBASE
on STN
AN 93041186 EMBASE
DN 1993041186
TI Comparative inhibition of extrinsic and intrinsic thrombin generation by standard heparin, a low molecular weight heparin and the synthetic ATIII-binding pentasaccharide.
AU Lormeau J.-C.; Herault J.-P.
CS Sanofi Recherche Centre Choay, 9, Avenue du Prdt Salvador Allende,94256 Gentilly Cedex, France
SO Thrombosis and Haemostasis, (1993) 69/2 (152-156+176).
ISSN: 0340-6245 CODEN: THHADQ
CY Germany
DT Journal; Article
FS 025 Hematology
030 Pharmacology

037 Drug Literature Index
LA English
SL English
AB The inhibiting effect of standard heparin, CY216 and the ATIII-binding synthetic pentasaccharide on extrinsic and intrinsic thrombin generation were quantified by evaluating the decrease of the total amount of active thrombin appearing in plasma after triggering coagulation. Heparin as well as CY216 produced the same quantitative inhibition of extrinsic and intrinsic TGs whereas pentasaccharide inhibited more efficiently extrinsic TG. This pattern of inhibition was further confirmed on pure extrinsic or intrinsic coagulation respectively in factor IX- and factor VII-depleted plasmas. Furthermore, selective suppression of the anti-thrombin activity of CY216 by limited amounts of PF4 affected the intrinsic TG inhibition more markedly than the extrinsic one. It was concluded that anticoagulant activity produced mainly through thrombin ***scavenging*** leads to similar quantitative impairment of extrinsic and intrinsic coagulation, while selective ATIII-mediated factor Xa inhibition results in a more marked effect against the extrinsic system.
SO Thrombosis and Haemostasis, (1993) 69/2 (152-156+176).
ISSN: 0340-6245 CODEN: THHADQ
AB The inhibiting effect of standard heparin, CY216 and the ATIII-binding synthetic pentasaccharide on extrinsic and intrinsic thrombin generation were quantified by evaluating the decrease of the total amount of active thrombin appearing in plasma after triggering coagulation. Heparin as well as CY216 produced the same quantitative inhibition of extrinsic and intrinsic TGs whereas pentasaccharide inhibited more efficiently extrinsic TG. This pattern of inhibition was further confirmed on pure extrinsic or intrinsic coagulation respectively in factor IX- and factor VII-depleted plasmas. Furthermore, selective suppression of the anti-thrombin activity of CY216 by limited amounts of PF4 affected the intrinsic TG inhibition more markedly than the extrinsic one. It was concluded that anticoagulant activity produced mainly through thrombin ***scavenging*** leads to similar quantitative impairment of extrinsic and intrinsic coagulation, while selective ATIII-mediated factor Xa inhibition results in a more marked effect against the extrinsic system.
CT Medical Descriptors:
*anticoagulation
article
blood clotting
priority journal
Drug Descriptors:
*antithrombin iii: EC, endogenous compound
*heparin: PD, pharmacology
*low molecular weight heparin: PD, pharmacology
*pentasaccharide: PD, pharmacology
*thrombin: EC, endogenous compound
blood clotting factor 10a
tissue factor pathway inhibitor: PD, pharmacology
nadroparin: PD, pharmacology
sr 90107: PD, pharmacology
thrombin inhibitor
thrombocyte factor 4: PD, pharmacology
unclassified drug
RN (antithrombin iii) 90170-80-2; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (thrombin) 9002-04-4; (blood clotting factor 10a) 72162-96-0, 9002-05-5; (***tissue*** ***factor*** ***pathway*** ***inhibitor***) 116638-34-7; (nadroparin) 104521-37-1; (thrombocyte factor 4) 37270-94-3, 69670-74-2

L7 ANSWER 12 OF 27 IFIPAT COPYRIGHT 2004 IFI on STN
AN 10203477 IFIPAT;IFIUDB;IFICDB
TI COMBINATIONS OF STEROL ABSORPTION INHIBITOR(S) WITH BLOOD MODIFIER(S) FOR TREATING VASCULAR CONDITIONS; ANTICHOLESTEROL AGENTS
INF Kosoglou; Teddy, Jamison, PA, US
Ress; Rudyard J., Flemington, NJ, US
Strony; John T., Lebanon, NJ, US
Veltri; Enrico P., Princeton, NJ, US
IN Kosoglou Teddy; Ress Rudyard J; Strony John T; Veltri Enrico P
PAF Schering Corporation
PA Schering Corp (74480)
AG SCHERING-PLOUGH CORPORATION PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530, US
PI US 2002147184 A1 20021010
AI US 2002-56680 20020125
PRAI US 2001-264275P 20010126 (Provisional)
US 2001-264396P 20010126 (Provisional)
US 2001-264600P 20010126 (Provisional)

US 2001-324123P 20010921 (Provisional)
FI US 2002147184 20021010
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 48
AB The present invention provides compositions, therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor; and (b) at least one blood modifier, which can be useful for treating vascular conditions and lowering plasma levels of sterols.
CLMN 48
PI US 2002147184 A1 20021010
ACLM 27. The composition according to claim 26, wherein the Factor Xa inhibitor is selected from the group consisting of disubstituted pyrazolines, disubstituted triazolines, substituted n-((aminoiminomethyl)phenyl)propylamides, substituted n-((aminomethyl)phenyl)propylamides, ***tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI), low molecular weight heparins, heparinoids, benzimidazolines, benzoxazolinones, benzopiperazinones, indanones, dibasic (amidinoaryl) propanoic acid derivatives, amidinophenyl-pyrrolidines, amidinophenyl-pyrrolines, amidinophenyl-isoxazolidines, amidinoindoles, amidinoazoles, bis-arlysulfonylaminobenzamide derivatives, peptidic Factor Xa inhibitors and combinations thereof.
42. The composition according to claim 1, further comprising at least one ***antioxidant*** or vitamin.

L7 ANSWER 13 OF 27 IFIPAT COPYRIGHT 2004 IFI on STN
AN 10193022 IFIPAT;IFIUDB;IFICDB
TI ARTERY SMOOTH MUSCLE- AND VEIN SMOOTH MUSCLE-SPECIFIC PROTEINS AND USES THEREFOR; METHOD FOR SELECTIVELY DELIVERING AGENT TO ARTERIAL SMOOTH MUSCLE CELLS IN MAMMAL COMPRISING ADMINISTERING AGENT AND SUBSTANCE WHICH SELECTIVELY BINDS ARTERIAL SMOOTH MUSCLE CELL-SPECIFIC SURFACE MOLECULE SELECTED FROM EPHRIN FAMILY
INF Anderson; David J., Atladena, CA, US
Garcia-Cardena; Guillermo, Boston, MA, US
Gimbrone; Michael A. JR., Jamaica Plain, MA, US
Wang; Hai U., Eldorado Hills, CA, US
IN Anderson David J; Garcia-Cardena Guillermo; Gimbrone Michael A JR; Wang Hai U
PAF California Institute of Technology, Pasadena, CA
PA California Institute of Technology (13190)
AG HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA 01742-9133, US
PI US 2002136726 A1 20020926
AI US 2001-988496 20011120
PRAI US 2000-252009P 20001120 (Provisional)
FI US 2002136726 20020926
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
GOVI (0002) The invention was supported by grant R37-HL51150 from the American Heart Association and grant P50-HL56985 from the National Heart, Lung and Blood Institute. The Government has certain rights in the invention.
CLMN 72
GI 4 Figure(s).
FIG. 1 is a diagram of the wild type locus of the EphrinB2 gene showing the Exon-1 structure. The filled box represents 5' untranslated region. The hatched box starts at the ATG, and includes the signal sequence. H=HindIII; X=XbaI; N=NcoI; E=EcoRI.
FIG. 2 is a diagram of the targeting vector used to disrupt the EphrinB2 gene.
FIG. 3 is a schematic representation of the mutated EphrinB2 locus.
FIG. 4 is a bar graph indicating the binding activity to GPIephrin-B2 of EphB2Fc in the presence of hamster anti-ephrin-B2 hybridoma supernatants.
AB Arterial and venous smooth muscle cells are molecularly distinct from the earliest stages of angiogenesis through to adulthood. This distinction is revealed by expression on arterial cells (e. g., arterial endothelial cells, arterial smooth muscle cells) of a transmembrane ligand, called EphrinB2 whose receptor EphB4 is expressed on venous cells. Targeted disruption of the EphrinB2 gene prevents the remodeling of veins from a capillary plexus into properly branched structures. Moreover, it also disrupts the remodeling of arteries, suggesting that reciprocal interactions between pre-specified arterial and venous cells are necessary for angiogenesis. Expression of EphrinB2 in arterial cells (e.g., arterial endothelial cells, arterial smooth muscle cells) can be used to advantage in methods for targeting agents and/or encoded

polypeptides to arterial smooth muscle cells, altering angiogenesis, assessing the effect of agents on arterial smooth muscle cells, identifying arterial smooth muscle cells, isolating arterial smooth muscle cells and production of artificial vessels, for example.

CLMN 72 4 Figure(s).

FIG. 1 is a diagram of the wild type locus of the EphrinB2 gene showing the Exon-1 structure. The filled box represents 5' untranslated region. The hatched box starts at the ATG, and includes the signal sequence. H=HindIII; X=XbaI; N=NcoI; E=EcoRI.

FIG. 2 is a diagram of the targeting vector used to disrupt the EphrinB2 gene.

FIG. 3 is a schematic representation of the mutated EphrinB2 locus.

FIG. 4 is a bar graph indicating the binding activity to GPIephrin-B2 of EphB2Fc in the presence of hamster anti-ephrin-B2 hybridoma supernatants.

PI US 2002136726 A1 20020926

ACLM 8. The method of claim 1 wherein said agent is selected from the group consisting of a cyclin G1 mutant polypeptide, a p27-p16 chimeric polypeptide, a hepatocyte growth factor, a herpes simplex virus thymidine kinase polypeptide, a cytosine deaminase-5-flurocytosine polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, a synthetic double-stranded nucleic acid with high binding affinity for E2F, an anti-sense oligonucleotide to p65, an anti-sense oligonucleotide to basic fibroblast growth factor, an active site inactivated factor VIIa polypeptide, a recombinant ***tissue*** ***factor*** ***pathway*** ***inhibitor*** , rapamycin, an ***antioxidant*** , a glycoprotein IIb/IIIa receptor antagonist, a calcium channel blocker and a nitric oxide donor.

44. The oligonucleotide of claim 42, wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** polypeptide.

46. The method of claim 45 wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** polypeptide.

51. The method of claim 49, wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** polypeptide.

64. The method of claim 60, wherein said second nucleic acid sequence encodes a polypeptide selected from the group consisting of a herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase

polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p 16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide and a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** polypeptide.

L7 ANSWER 14 OF 27 IFIPAT COPYRIGHT 2004 IFI on STN
AN 10082677 IFIPAT;IFIUDB;IFICDB
TI DELIVERY SYSTEMS FOR PERIADVENTITIAL DELIVERY FOR TREATMENT OF RESTENOSIS AND ANASTOMOTIC INTIMAL HYPERPLASIA
INF Cunanan; Crystal M., Mission Viejo, CA, US
Helmus; Michael N., Worcester, MA, US
Tremble; Patrice, Santa Rosa, CA, US
IN Cunanan Crystal M; Helmus Michael N; Tremble Patrice
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
PPA Edwards Lifesciences Corp (Probable)
AG Debra D. Condino, Esq. Edwards Lifesciences Corp., c/o Edwards Lifesciences LLC, One Edwards Way, Irvine, CA, 92614, US
PI US 2002026236 A1 20020228
AI US 2001-771480 20010125
PRAI US 2000-178087P 20000125 (Provisional)
FI US 2002026236 20020228
US 6730313 20040504
DT Utility; Patent Application - First Publication
FS MECHANICAL
APPLICATION
CLMN 66
AB The invention provides methods for treating injuries to one or more internal structures of a subject by administering a drug delivery vehicle to an external surface of the injured structure. The drug delivery vehicle substantially adheres to the site of administration and provides for the release of a bioactive agent that reduces or prevents further injury to the internal structure by disease processes, such as hyperplasia.
CLMN 66
PI US 2002026236 A1 20020228
ACLM 11. The method according to claim 1, wherein said intimal hyperplasia preventing agent is a member selected from antithrombotics, antiinflammatories, corticosteroids, antimicrotubule agents, antisense oligonucleotides, antineoplaastics, ***antioxidants*** , antiplatelets, calcium channel blockers, converting enzyme inhibitors, cytokine inhibitors, growth factors, growth factor inhibitors, growth factor sequestering agents, fibrosis inhibitors, immunosuppressives, ***tissue*** ***factor*** ***inhibitor*** , smooth muscle inhibitors, sulfated proteoglycans, superoxide dismutase mimics, NO, NO precursors and combinations thereof.
40. The method according to claim 35, wherein said intimal hyperplasia preventing agent is a member selected from antithrombotics, antiinflammatories, corticosteroids, antimicrotubule agents, antisense oligonucleotides, antineoplaastics, ***antioxidants*** , antiplatelets, calcium channel blockers, converting enzyme inhibitors, cytokine inhibitors, growth factors, growth factor inhibitors, growth factor sequestering agents, fibrosis inhibitors, immunosuppressives, ***tissue*** ***factor*** ***inhibitor*** , smooth muscle inhibitors, sulfated proteoglycans, superoxide dismutase mimics, NO, NO precursors and combinations thereof.
57. The method according to claim 48, wherein said intimal hyperplasia preventing agent is a member selected from antithrombotics, antiinflammatories, corticosteroids, antimicrotubule agents, antisense oligonucleotides, antineoplaastics, ***antioxidants*** , antiplatelets, calcium channel blockers, converting enzyme growth factor sequestering agents, cytokine inhibitors, growth factors, growth factor inhibitors, fibrosis inhibitors, immunosuppressives, ***tissue*** ***factor*** ***inhibitor*** , smooth muscle inhibitors, sulfated proteoglycans, superoxide dismutase mimics, NO, NO precursors and combinations thereof.

L7 ANSWER 15 OF 27 MEDLINE on STN
AN 95132671 MEDLINE
DN PubMed ID: 7831358
TI Studies on the inflammatory-coagulant axis in the baboon response to E. coli: regulatory roles of proteins C, S, C4bBP and of inhibitors of tissue factor.

AU Taylor F B Jr
CS Cardiovascular Biology Research Program, Oklahoma Medical Research Foundation, Oklahoma City 73104.
SO Progress in clinical and biological research, ***(1994)*** 388 175-94.
Ref: 13
Journal code: 7605701. ISSN: 0361-7742.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199502
ED Entered STN: 19950307
Last Updated on STN: 19950307
Entered Medline: 19950217
AB The baboon model of E. coli sepsis illustrates three concepts with respect to the host response and vascular endothelium. First, the endothelium is the primary target. E. coli sepsis is an acute inflammatory disease of the vascular endothelium. Second, the endothelium is not a passive target. Initially it regulates both the inflammatory and coagulopathic aspects of E. coli sepsis through membrane associated regulatory receptor/plasma protein assemblies including protein C/thrombomodulin, activated protein C/protein S, C4bBP/protein S, ***tissue*** ***factor*** ***pathway*** ***inhibitor*** /Xa, antithrombin III/glycosaminoglycans. Third, when overridden by inflammatory events, the endothelium can change its anticoagulant phenotype and mount a massive procoagulant fibrinolytic counter-attack on its luminal side through the expression of tissue factor and release of tissue plasminogen activator. Fourth, again when overridden by inflammatory events, the endothelium can change its ***antioxidant*** phenotype and produce a "distal" tissue hypoxia on its abluminal side through induction of free radical generation and peroxidation of mitochondrial lipid membranes of those tissues with high metabolic rates. It has become increasingly clear that the so-called anticoagulant systems which act on the proximal factors of the clotting cascade (protein C, TFPI, AT-III, PGI2) also attenuate the amplification of the inflammatory response. Aspects of the mechanism by which this occurs are coming to light. This includes the attenuation of Il-6 response by TFPI and the attenuation of the complement effects by C4bBP/PS. The specifics of these observations in the E. coli sepsis model will be reviewed.
SO Progress in clinical and biological research, ***(1994)*** 388 175-94.
Ref: 13
Journal code: 7605701. ISSN: 0361-7742.
AB The baboon model of E. coli sepsis illustrates three concepts with respect to the host response and vascular endothelium. First, the endothelium is the primary target. E. coli sepsis is an acute inflammatory disease of the vascular endothelium. Second, the endothelium is not a passive target. Initially it regulates both the inflammatory and coagulopathic aspects of E. coli sepsis through membrane associated regulatory receptor/plasma protein assemblies including protein C/thrombomodulin, activated protein C/protein S, C4bBP/protein S, ***tissue*** ***factor*** ***pathway*** ***inhibitor*** /Xa, antithrombin III/glycosaminoglycans. Third, when overridden by inflammatory events, the endothelium can change its anticoagulant phenotype and mount a massive procoagulant fibrinolytic counter-attack on its luminal side through the expression of tissue factor and release of tissue plasminogen activator. Fourth, again when overridden by inflammatory events, the endothelium can change its ***antioxidant*** phenotype and produce a "distal" tissue hypoxia on its abluminal side through induction of free radical generation and peroxidation of mitochondrial lipid membranes of those tissues with high metabolic rates. It has become increasingly clear that the so-called anticoagulant systems which act on the proximal factors of the clotting cascade (protein C, TFPI, AT-III, PGI2) also attenuate the amplification of the inflammatory response. Aspects of the mechanism by which this occurs are coming to light. This includes the attenuation of Il-6 response by TFPI and the attenuation of the complement effects by C4bBP/PS. The specifics of these observations in the E. coli sepsis model will be reviewed.

L7 ANSWER 16 OF 27 MEDLINE on STN
AN 90274446 MEDLINE
DN PubMed ID: 1693492
TI A baboon model for pregnancy-associated antigens (PAPP-A, PP5, PP14).
AU Sinosich M J; Pope V Z; Pope C E; Beck L R; Teisner B; Saunders D M
CS Department of Obstetrics and Gynaecology, Royal North Shore Hospital, St. Leonards, Australia.

SO Archives of gynecology and obstetrics, ***(1990)*** 247 (2) 53-62.
Journal code: 8710213. ISSN: 0932-0067.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199007
ED Entered STN: 19900810
Last Updated on STN: 19960129
Entered Medline: 19900711
AB By radioimmunoassays established on human derived antigens, PAPP-A, PP5 and PP14 immunoreactivity was detected in placental extracts and blood of pregnant baboons. None of the serial dilution curves suggested parallelism between respective human and baboon samples. Based on slopes of regressed logit-log transformed binding data, PAPP-A demonstrated the greatest degree of interspecies immunological crossreactivity. PP14 showed the least conservation of antigenic determinants. Physicochemical characterization on heparin, zinc ***chelate*** and bovine thrombin affinity matrices could not distinguish human from baboon-derived antigens. As in the human, baboon PAPP-A and PP5 were not detected in blood of male or non-pregnant animals. PP14 was detected in baboon follicular fluid, and only PP5 immunoreactivity was measured in culture media of baboon embryos. Of the three antigens, PAPP-A was detected in pregnant baboons at about 61 days gestation, that is, 4 weeks before PP5 and PP14. With the exception of PP14 which attained peak concentration at 118 days of pregnancy, PAPP-A and PP5 concentrations were greatest at term. In conjunction with physicochemical and immunological criteria, these physiological kinetics clearly support a role for developing a baboon model to serve for further studies into feto-maternal signals, particularly antigens such as PAPP-A and PP5.
SO Archives of gynecology and obstetrics, ***(1990)*** 247 (2) 53-62.
Journal code: 8710213. ISSN: 0932-0067.
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CN 0 (Glycoproteins); 0 (Histocompatibility Antigens); 0 (Histocompatibility Antigens Class I); 0 (PAEP protein, human); 0 (Pregnancy Proteins); 0 (pregnancy-specific antigen, sheep); 0 (***tissue*** - ***factor*** - ***pathway*** ***inhibitor*** 2); EC 3.4.24.- (Pregnancy-Associated Plasma Protein-A)

L7 ANSWER 17 OF 27 MEDLINE on STN
AN 88295409 MEDLINE
DN PubMed ID: 3402060
TI Immunofluorometric demonstration and quantification of placental protein 5 in the absence of pregnancy.
AU Butzow R; Alfthan H; Stenman U H; Suikkari A M; Bohn H; Seppala M
CS First Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Finland.
SO Clinical chemistry, ***(1988 Aug)*** 34 (8) 1591-3.
Journal code: 9421549. ISSN: 0009-9147.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198809
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880922
AB This time-resolved immunofluorometric assay (IFMA) developed for

measurement of placental protein 5 (PP5) involves two antibodies: a monoclonal anti-PP5 antibody attached to a solid phase and an europium(III) ***chelate*** -labeled polyclonal anti-PP5 antibody as a tracer. The measuring range is 0.05-100 micrograms/L and the detection limit is 20 times lower than that of a PP5 radioimmunoassay (RIA) performed with the same polyclonal antiserum. By IFMA, PP5 could be detected and quantified in all plasma and serum samples of nonpregnant and pregnant individuals, whereas PP5 was undetectable by RIA in serum of healthy men and nonpregnant women. The mean concentration of PP5 in sera from men was 0.43 micrograms/L (SD 0.13, range 0.19-0.75, n = 47) and in sera from nonpregnant women 0.49 micrograms/L (SD 0.19, range 0.20-0.90, n = 41). PP5 concentrations in serum showed no systematic variation during the menstrual cycle. In serum samples from 60 pregnant women the results obtained by IFMA and RIA correlated well (r = 0.97).

SO Clinical chemistry, ***(1988 Aug)*** 34 (8) 1591-3.
Journal code: 9421549. ISSN: 0009-9147.

AB This time-resolved immunofluorometric assay (IFMA) developed for measurement of placental protein 5 (PP5) involves two antibodies: a monoclonal anti-PP5 antibody attached to a solid phase and an europium(III) ***chelate*** -labeled polyclonal anti-PP5 antibody as a tracer. The measuring range is 0.05-100 micrograms/L and the detection limit is 20 times lower than that of a PP5 radioimmunoassay (RIA) performed with the same polyclonal antiserum. By IFMA, PP5 could be detected and quantified in all plasma and serum samples of nonpregnant and pregnant individuals, whereas PP5 was undetectable by RIA in serum of healthy men and nonpregnant women. The mean concentration of PP5 in sera from men was 0.43 micrograms/L (SD 0.13, range 0.19-0.75, n = 47) and in sera from nonpregnant women 0.49 micrograms/L (SD 0.19, range 0.20-0.90, n = 41). PP5 concentrations in serum showed no systematic variation during the menstrual cycle. In serum samples from 60 pregnant women the results obtained by IFMA and RIA correlated well (r = 0.97).

CN 0 (Glycoproteins); 0 (Pregnancy Proteins); 0 (***tissue*** - ***factor*** - ***pathway*** ***inhibitor*** 2)

L7 ANSWER 18 OF 27 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AN 2001:12312 SCISEARCH

GA The Genuine Article (R) Number: 385VC

TI Oxidized low-density lipoprotein impairs the anti-coagulant function of ***tissue*** - ***factor*** - ***pathway*** ***inhibitor*** through oxidative modification by its high association and accelerated degradation in cultured human endothelial cells

AU Horie S (Reprint); Hiraishi S; Hirata Y; Kazama M; Matsuda J

CS Teikyo Univ, Fac Pharmaceut Sci, Dept Clin Biochem, 1091-1 Suarashi, Kanagawa 1990195, Japan (Reprint); Teikyo Univ, Fac Pharmaceut Sci, Dept Clin Biochem, Kanagawa 1990195, Japan

CYA Japan

SO BIOCHEMICAL JOURNAL, (***1 DEC 2000***) Vol. 352, Part 2, pp. 277-285.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON W1N 3AJ, ENGLAND.
ISSN: 0264-6021.

DT Article; Journal

LA English

REC Reference Count: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have examined whether oxidized low-density lipoprotein (ox-LDL) affects the function of ***tissue*** - ***factor*** - ***pathway*** ***inhibitor*** (TFPI), an anti-coagulant regulator in the extrinsic pathway of coagulation, in cultured human umbilical vein endothelial cells (HUVEC). Treatment of culture medium of HUVEC with ox-LDL, but not with native or acetylated LDLs, drastically decreased the reactivity of TFPI to its antibody specific for Kunitz domain 1 or one specific for the conformation between Kunitz 1 and 2 of TFPI, and caused a rapid, concentration-dependent decrease in the functional activity of TFPI to inhibit Factor X activation. When 5 ng of recombinant TFPI (rTFPI) was mixed with 10 mug of ox-LDL for 30 min, almost all of the rTFPI was detected in the ox-LDL fraction and no free rTFPI was observed on non-denaturing PAGE, in contrast with the virtual absence of rTFPI in the native LDL fraction. Ox-LDL decreased the antigen level of TFPI in the lysate of HUVEC in a time-dependent manner. It did not affect the mRNA level, but ox-LDL-dependent reduction of the TFPI antigen level in HUVEC was reversed by the simultaneous treatment of ox-LDL with bafilomycin A1, an inhibitor of the lysosomal proton pump. These results indicate that ox-LDL lessens the anti-coagulant function of TFPI through both oxidative modification and accelerated degradation of the molecule outside and inside HUVEC respectively.

TI Oxidized low-density lipoprotein impairs the anti-coagulant function of ***tissue*** - ***factor*** - ***pathway*** ***inhibitor***

through oxidative modification by its high association and accelerated degradation in cultured human endothelial cells

SO BIOCHEMICAL JOURNAL, (***1 DEC 2000***) Vol. 352, Part 2, pp. 277-285. Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON W1N 3AJ, ENGLAND. ISSN: 0264-6021.

AB We have examined whether oxidized low-density lipoprotein (ox-LDL) affects the function of ***tissue*** - ***factor*** - ***pathway*** ***inhibitor*** (TFPI), an anti-coagulant regulator in the extrinsic pathway of coagulation, in cultured human umbilical vein endothelial cells (HUVEC). Treatment of culture medium of HUVEC with ox-LDL, but not with native or acetylated LDLs, drastically decreased the reactivity of TFPI to its antibody specific for Kunitz domain 1 or one specific for the conformation between Kunitz 1 and 2 of TFPI, and caused a rapid, concentration-dependent decrease in the functional activity of TFPI to inhibit Factor X activation. When 5 ng of recombinant TFPI (rTFPI) was mixed with 10 mug of ox-LDL for 30 min, almost all of the rTFPI was detected in the ox-LDL fraction and no free rTFPI was observed on non-denaturing PAGE, in contrast with the virtual absence of rTFPI in the native LDL fraction. Ox-LDL decreased the antigen level of TFPI in the lysate of HUVEC in a time-dependent manner. It did not affect the mRNA level, but ox-LDL-dependent reduction of the TFPI antigen level in HUVEC was reversed by the simultaneous treatment of ox-LDL with bafilomycin A1, an inhibitor of the lysosomal proton pump. These results indicate that ox-LDL lessens the anti-coagulant function of TFPI through both oxidative modification and accelerated degradation of the molecule outside and inside HUVEC respectively.

STP KeyWords Plus (R): FAMILIAL HYPERCHOLESTEROLEMIA; EXPRESSION CLONING; ***SCAVENGER*** RECEPTOR; LIPID-PEROXIDATION; HUMAN PLASMA; LDL; ATHEROSCLEROSIS; COMPLEX; CHOLESTEROL; PROTEIN

L7 ANSWER 19 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-058418 [05] WPIDS

DNC C2003-014913

TI Measuring coagulation of blood for assessing the over-all coagulant properties of blood, comprises inhibiting activation of the intrinsic contact activation pathway of coagulation and activating the extrinsic coagulation pathway.

DC B04 S16

IN BENECKY, M J; MOSKOWITZ, K A; POST, D R; BENECKY, M; MOSKOWITZ, K; POST, D

PA (BEN-I) BENECKY M J; (MOSK-I) MOSKOWITZ K A; (POST-I) POST D R; (COAG-N) COAGULATION DIAGNOSTICS INC

CYC 10

PI WO 2002079375 A1 20021010 (200305)* EN 55<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003064414 A1 20030403 (200325)
AU 2002258643 A1 20021015 (200432) <--

ADT WO 2002079375 A1 WO 2002-US9584 20020329; US 2003064414 A1 Provisional US 2001-279737P 20010330, US 2002-107409 20020328; AU 2002258643 A1 AU 2002-258643 20020329

FDT AU 2002258643 A1 Based on WO 2002079375

PRAI US 2001-279737P 20010330; US 2002-107409 20020328

AN 2003-058418 [05] WPIDS

AB WO 200279375 A UPAB: 20030121
NOVELTY - Measuring coagulation of blood comprises inhibiting the activation of the intrinsic contact activation pathway of coagulation and activating the extrinsic activation pathway of coagulation.
DETAILED DESCRIPTION - Measuring coagulation of blood comprises:
(a) obtaining blood from a mammal;
(b) inhibiting in vitro activation of the intrinsic contact activation pathway of coagulation in the blood;
(c) initiating activation of the extrinsic activation pathway of coagulation by contacting the blood with at least 1 pro-coagulant; and
(d) measuring coagulation of the blood.
INDEPENDENT CLAIMS are also included for:
(1) a method for measuring the effectiveness of at least 1 coagulation factor or coagulation inhibitor on the coagulation of blood, comprising:
(a) obtaining blood from a mammal;
(b) dividing the blood into at least two aliquots;
(c) treating the first aliquot by:
(i) inhibiting in vitro activation of the intrinsic contact activation pathway of coagulation;

(ii) initiating activation of the extrinsic activation pathway of coagulation by contacting the first aliquot with a pro-coagulant; and
(iii) measuring coagulation of the first aliquot;
(d) treating the second aliquot by:
(i) inhibiting in vitro activation of the intrinsic contact activation pathway of coagulation in vitro;
(ii) contacting the second aliquot with the at least 1 coagulation factor or coagulation inhibitor;
(iii) initiating activation of the extrinsic activation pathway of coagulation by contacting the second aliquot with at least 1 pro-coagulant; and
(iv) measuring coagulation of the second aliquot; and
(e) comparing coagulation measurements of the first and second aliquots;
(2) a blood collection apparatus comprising a vessel that contains a contact activation pathway inhibitor; and
(3) a method for monitoring recovery of a patient from a condition related to abnormal blood coagulation, comprising:
(a) obtaining at least two blood samples from a patient;
(b) inhibiting activation of the intrinsic contact activation pathway of coagulation in the blood samples;
(c) initiating activation of the extrinsic activation pathway of coagulation by contacting the blood samples with at least 1 pro-coagulant;
(d) measuring coagulation of the blood (1 of the blood samples is obtained before administration of medical treatment or a surgical procedure, and the other blood samples are obtained during or after administration of the medical treatment or the surgical procedure).
USE - The methods are useful in rapidly assessing the over-all coagulant properties of a patient's blood sample. The methods are also useful for measuring the risk of a patient for a thrombotic event and for monitoring the effectiveness of pro-coagulant/anticoagulant therapy. The methods can also be used to determine the effective dose of a particular pro-coagulant or anticoagulant medication.
ADVANTAGE - The present method provides a rapid and simple in vitro assessment of the over-all coagulability of whole blood that is more representative of the physiological coagulation cascade, unlike prior art methods, which uses plasma, which does not contain activated platelets and platelets.
Dwg.0/0

PI WO 2002079375 A1 20021010 (200305)* EN 55 C12M001-34 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003064414 A1 20030403 (200325) G01N033-567
AU 2002258643 A1 20021015 (200432) C12M001-34 <--
ADT WO 2002079375 A1 WO 2002-US9584 20020329; US 2003064414 A1 Provisional US 2001-279737P 20010330, US 2002-107409 20020328; AU 2002258643 A1 AU 2002-258643 20020329
AU 2002258643 A1 Based on WO 2002079375
PRAI US 2001-279737P 20010330; US 2002-107409 20020328
UPTX: 20030121

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: In measuring coagulation of blood, the blood is contacted with a surface of low thrombogenic activity (e.g. plastic or siliconized glass).
Inhibiting activation of the intrinsic contact activation pathway of coagulation comprises contacting the blood with at least 1 contact activation pathway inhibitor, which is a Factor XIIa inhibitor, a Factor XIa inhibitor, or a kallikrein inhibitor. The Factor XIIa inhibitor is corn trypsin inhibitor, an antibody to Factor XIIa, CI-esterase inhibitor, or a XIIa-binding peptide. The kallikrein inhibitor is aprotinin, an antibody to kallikrein, CI-esterase inhibitor, or a kallikrein-binding peptide. The pro-coagulant is Factor VIIa, Factor IXa, Factor Xa, Factor XIa, viper venom, lipidated tissue factor, apo-tissue factor, or recombinant soluble tissue factor. Factor VIIa is added at a final concentration ranging from about 5-100 nanomoles/L in the blood. Factor VIIa is a recombinant Factor VIIa, natural Factor VIIa, or lipidated Factor IIa.
Inhibiting activation of the intrinsic contact activation pathway of coagulation comprises:
(a) contacting the blood with a surface having a low thrombogenic activity, or with corn trypsin inhibitor (initiating activation of the extrinsic activation pathway of coagulation comprises contacting the blood with Factor VIIa, Factor IXa, Factor Xa, Factor XIa, viper venom,

lipidated tissue factor, apo-tissue factor, or recombinant soluble tissue factor); or
(b) contacting the blood with aprotinin or CI-esterase inhibitor (initiating activation of the extrinsic activation pathway of coagulation comprises contacting the blood with plasma or recombinant Factor VIIa, Factor IXa, Factor Xa, Factor XIa, viper venom, thrombin, lipidated tissue factor, apo- tissue factor, or soluble recombinant tissue factor).
The method further comprises:
(a) adding at least 1 anti-platelet agent to the blood, where the anti-platelet agent is aspirin, NSAIDS, dipyridamole, ticlopidine, clopidogrel, adenosine, theophylline, or a glycoprotein IIb/IIIa antagonist;
(b) comparing coagulation of the blood to reference data defining a range of normal coagulation; or
(c) comparing coagulation of the blood to coagulation of a control sample (the control sample has been treated with a known amount of a coagulation factor or inhibitor).
Inhibition of the intrinsic contact activation pathway occurs concurrently with activation of the extrinsic activation pathway. The blood has not been treated to prevent clotting, or has been citrated and recalcified. Factor XIa inhibitor is an antibody to factor XI, CI-esterase inhibitor, or a Factor XIa-binding peptide, where the antibody is a monoclonal antibody. The glycoprotein IIb/IIIa antagonist is abciximab, eptifibatide, or tirofiban. A coagulation inhibitor is administered to the mammal before the blood is obtained, where the coagulation inhibitor is low molecular weight heparin, UFH, pentasaccharide, a direct thrombin inhibitor, a direct factor Xa inhibitor, a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** , a Factor IX inhibitor, activated protein C, or ATIII.
Measuring the effectiveness of at least 1 coagulation factor or coagulation inhibitor on coagulation of a blood sample, comprises:
(a) obtaining a first blood sample from a mammal;
(b) inhibiting activation of the intrinsic contact activation pathway of coagulation;
(c) initiating activation of the extrinsic activation pathway of coagulation by contacting the first blood sample with a pro-coagulant agent;
(d) measuring coagulation of the first blood sample;
(e) obtaining a second blood sample from the mammal;
(f) inhibiting activation of the intrinsic contact activation pathway of coagulation;
(g) contacting the second blood sample with at least 1 coagulation factor or inhibitor;
(h) initiating activation of the extrinsic pathway of coagulation by contacting the second blood sample with at least 1 pro-coagulant;
(i) measuring coagulation of the second blood sample; and
(j) comparing coagulation measurements of the first and second blood samples.
Coagulation factor or coagulation inhibitor is administered to the mammal before the second blood sample is obtained. The method further comprises:
(a) adjusting the concentration of at least 1 coagulation factor or coagulation inhibitor in the mammal after the coagulation measurements are compared; or
(b) administering at least 1 second coagulation factor or coagulation inhibitor to the mammal after the coagulation measurements are compared.
The blood has not been treated to prevent clotting, or has been citrated and recalcified. The pro-coagulant is lipidated tissue factor and the contact activation pathway inhibitor is aprotinin. The ***tissue*** ***factor*** ***pathway*** ***inhibitor*** is TFPI, VIIai, rNAPc2, anti-tissue factor monoclonal antibody, soluble AA mutated tissue factor, or coumadin. The Factor IX inhibitor is an anti-Factor IX monoclonal antibody or FIXai.
Preferred Apparatus: The vessel is an evacuated tube. The apparatus further comprises a Ca2+ ***chelator*** .

L7 ANSWER 20 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-643334 [69] WPIDS
CR 2002-643328 [69]; 2002-643332 [69]; 2002-643333 [69]; 2002-691526 [74]
DNC C2004-014190
TI Composition useful for e.g. treating vascular conditions (hyperlipidemia), diabetes, obesity or lowering a concentration of a sterol in plasma of a mammal, comprises sterol absorption inhibitor and blood modifier.
DC B03 B05
IN KOSOGLOU, T; RESS, R J; STRONY, J; VELTRI, E P; STRONY, J T
PA (SCHE) SCHERING CORP
CYC 98
PI WO 2002058734 A2 20020801 (200269)* EN 103<--

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            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM
            DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT
            LU LV MA MD MG MK MN MX MZ NO NZ PH PL PT RO RU SE SG SI SK SL TJ
            TM TN TR TT TZ UA UZ VN YU ZA ZM
      US 2002147184    A1 20021010 (200269)          <--
      EP 1353694       A2 20031022 (200370)  EN
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
      NO 2003003357    A  20030925 (200373)
      SK 2003000950    A3 20031201 (200404)
      BR 2002006639    A  20040225 (200416)
      HU 2003003917    A2 20040301 (200422)
      AU 2002237927    A1 20020806 (200427)          <--
      CZ 2003002039    A3 20040114 (200429)
      JP 2004517920    W  20040617 (200440)       192
      KR 2004025890    A  20040326 (200446)
ADT   WO 2002058734 A2 WO 2002-US2013 20020125; US 2002147184 A1 Provisional US
      2001-264275P 20010126, Provisional US 2001-264396P 20010126, Provisional
      US 2001-264600P 20010126, Provisional US 2001-324123P 20010921, US
      2002-56680 20020125; EP 1353694 A2 EP 2002-704233 20020125, WO 2002-US2013
      20020125; NO 2003003357 A WO 2002-US2013 20020125, NO 2003-3357 20030725;
      SK 2003000950 A3 WO 2002-US2013 20020125, SK 2003-950 20020125; BR
      2002006639 A BR 2002-6639 20020125, WO 2002-US2013 20020125; HU 2003003917
      A2 WO 2002-US2013 20020125, HU 2003-3917 20020125; AU 2002237927 A1 AU
      2002-237927 20020125; CZ 2003002039 A3 WO 2002-US2013 20020125, CZ
      2003-2039 20020125; JP 2004517920 W JP 2002-559068 20020125, WO
      2002-US2013 20020125; KR 2004025890 A KR 2003-709794 20030724
FDT   EP 1353694 A2 Based on WO 2002058734; SK 2003000950 A3 Based on WO
      2002058734; BR 2002006639 A Based on WO 2002058734; HU 2003003917 A2 Based
      on WO 2002058734; AU 2002237927 A1 Based on WO 2002058734; CZ 2003002039
      A3 Based on WO 2002058734; JP 2004517920 W Based on WO 2002058734
PRAI  US 2001-324123P      20010921; US 2001-264275P      20010126;
      US 2001-264396P      20010126; US 2001-264600P      20010126;
      US 2002-56680        20020125
AN    2002-643334 [69]   WPIDS
CR    2002-643328 [69]; 2002-643332 [69]; 2002-643333 [69]; 2002-691526 [74]
AB    WO 200258734 A UPAB: 20040720
      NOVELTY - A composition comprises at least one sterol absorption inhibitor
      and at least one blood modifier.
           ACTIVITY - Antilipemic; Antidiabetic; Anorectic; Antiarteriosclerotic;
       Hypotensive; Antiinflammatory; Cerebroprotective; Antianginal; Cardiant;
      Anticoagulant.
           MECHANISM OF ACTION - Sterol absorption inhibitor; Platelet function
      inhibitor.
           USE - For the treatment or prevention of vascular condition
      (hyperlipidemia), diabetes, obesity or lowering a concentration of a
      sterol in plasma of a mammal (all claimed). Also for treating
      atherosclerosis, hypercholesterolemia, hypertriglyceridaemia,
      sitosterolemia, vascular inflammation, hypertension, angina, cardiac
      arrhythmias or stroke.
           ADVANTAGE - By using combination therapy, the side effects of
      individual compounds can be reduced compared to monotherapy, which
      improves patient compliance and provides a broader range of complimentary
      effects or modes of action.
      Dwg.0/0
PI    WO 2002058734    A2 20020801 (200269)* EN  103     A61K045-06     <--
         RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
             NL OA PT SD SE SL SZ TR TZ UG ZM ZW
          W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CZ DE DK DM
             DZ EC EE ES FI GB GD GE HR HU ID IL IN IS JP KG KR KZ LC LK LR LT
             LU LV MA MD MG MK MN MX MZ NO NZ PH PL PT RO RU SE SG SI SK SL TJ
             TM TN TR TT TZ UA UZ VN YU ZA ZM
      US 2002147184    A1 20021010 (200269)          A61K031-397    <--
      EP 1353694       A2 20031022 (200370)  EN      A61K045-06
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
      NO 2003003357    A  20030925 (200373)          A61K045-06
      SK 2003000950    A3 20031201 (200404)          A61K045-06
      BR 2002006639    A  20040225 (200416)          A61K045-06
      HU 2003003917    A2 20040301 (200422)          A61K045-06
      AU 2002237927    A1 20020806 (200427)          A61K045-06     <--
      CZ 2003002039    A3 20040114 (200429)          A61K045-06
      JP 2004517920    W  20040617 (200440)       192 A61K045-06
      KR 2004025890    A  20040326 (200446)          A61K031-397
ADT   WO 2002058734 A2 WO 2002-US2013 20020125; US 2002147184 A1 Provisional US
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2001-264275P 20010126, Provisional US 2001-264396P 20010126, Provisional US 2001-264600P 20010126, Provisional US 2001-324123P 20010921, US 2002-56680 20020125; EP 1353694 A2 EP 2002-704233 20020125, WO 2002-US2013 20020125; NO 2003003357 A WO 2002-US2013 20020125, NO 2003-3357 20030725; SK 2003000950 A3 WO 2002-US2013 20020125, SK 2003-950 20020125; BR 2002006639 A BR 2002-6639 20020125, WO 2002-US2013 20020125; HU 2003003917 A2 WO 2002-US2013 20020125, HU 2003-3917 20020125; AU 2002237927 A1 AU 2002-237927 20020125; CZ 2003002039 A3 WO 2002-US2013 20020125, CZ 2003-2039 20020125; JP 2004517920 W JP 2002-559068 20020125, WO 2002-US2013 20020125; KR 2004025890 A KR 2003-709794 20030724

FDT EP 1353694 A2 Based on WO 2002058734; SK 2003000950 A3 Based on WO 2002058734; BR 2002006639 A Based on WO 2002058734; HU 2003003917 A2 Based on WO 2002058734; AU 2002237927 A1 Based on WO 2002058734; CZ 2003002039 A3 Based on WO 2002058734; JP 2004517920 W Based on WO 2002058734

PRAI US 2001-324123P 20010921; US 2001-264275P 20010126;
US 2001-264396P 20010126; US 2001-264600P 20010126;
US 2002-56680 20020125

TECH UPTX: 20040429

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compound: The sterol absorption inhibitor is of formula (I), (II), (VIIA), (VIIB), salts, solvates, prodrugs or their isomers.

U = Ar2, Ar'2, Ar2, Ar'3, Ar2;

U' = Ar3, Ar'3, phenyl (substituted by A' and R19), Ar'2, A-B', phenyl (substituted by -O-G and at position 2 by R26) or phenyl (substituted by R26);

U'' = Zp-(C)r(R2)(R3)-Yn-(C)q(R)(R1)-Xm-Ar1, Zp-C(R'1)(R'2)-Yq'-A-Ar'1, Q-R1-Ar1, S(O)r-Yn'-(C)q'(R)(R1)-Xm'-Ar'1, Q'-R1-Ar1 or Q-CH(OR'1)-Ar'1;

Ar1 and Ar2 = aryl (optionally mono- to penta-substituted by R4);

Ar3 = aryl (optionally mono- to penta-substituted by R5);

X, Y and Z = CH2, CH(lower alkyl) or C(dilower alkyl);

R, R2 and R'1 = OR6, O(CO)R6, O(CO)OR9 or O(CO)NR6R7;

R1, R3 and R'2 = H, lower alkyl or aryl;

q, r, s and v = 0 or 1;

m, n, p and h = 0 - 4;

m+n+p+q+r and f+g = 1 - 6;

m+n+q, f, j, k and j+k+v = 1 - 5;

R4 = T, lower alkyl, -O(CH2)1-5OR6, NR6SO2R9, COOR6, S(O)0-2R9, CF3, CN, NO2 or halo;

R5 = T, O(CH2)1-5OR6, NR6SO2R9, COOR6 or -S(O)0-2R9;

T = OR6, -O(CO)R6, -O(CO)OR9, -O(CO)NR6R7, -NR6R7, -NR6(CO)R7, -NR6(CO)OR9, -NR6(CO)NR7R8, -CONR6R7, -COR6, -SO2NR6R7, O(CH2)110-COOR6, -O(CH2)1-10CONR6R7, -(lower alkylene)COOR6 or -CH=CH-COOR6;

R6 - R8 = lower alkyl (optionally substituted by aryl), H or aryl;

R9 = lower alkyl (optionally substituted by aryl) or aryl;

Ar'1 = aryl (mono- to tri- substituted by R'3);

Ar'2 = aryl (mono - to tri-substituted by R'4);

Ar'3 = aryl (mono- to tri-substituted by R'5);

A = O, S, S(O) or -S(O)2;

R'1+R'2 = =O;

q' and d = 1 - 3;

R'5 = T, -O(CH2)1-5OR9, NR6SO2-lower alkyl, NR6SO2-aryl, S(O)0-2-alkyl, S(O)0-2-aryl, o-halogen, m-halogen, o-lower alkyl and m-lower alkyl;

R'3 and R'4 = R'5, H, p-lower alkyl, aryl, NO2, CF3 or p-halogen;

A' = heterocycloalkyl, heteroaryl, benzofused heterocycloalkyl or benzofused heteroaryl (all mono- to tri-substituted by R2);

Ar1 = aryl (optionally mono- to tri-substituted by R3);

Ar2 = aryl (optionally mono- to tri-substituted by R4);

Q = a bond or a group of formula (Ia);

R1 = (CH2)q, (CH2)e-G-(CH2)r', (2-6C) alkenylene-, -(CH2)f-V-(CH2)g or A1;

A1 = MY'd-C(R10)(R11)-Z'h, X'm-(C)s(R12)(R13)-Y'n-(C)t(R10)(R11)-Z'p or -X'j-(C)v(R10)(R11)-Y'k-S(O)0-2;

q = 2 - 6;

G = O, C(O), phenylene, NR8 or S(O)0-2;

e, r', g, m' and n' = 0 - 5;

e+r', q, a', b', d', a'+b'+d' and s' = 0 - 6;

V = 3-6C cycloalkylene;

R5 = CH, C(1-6C alkyl), CF, C(OH), C(C6H4-R'9), N or N+O-;

R'6 and R'7 = CH2, CH(1-6C alkyl), C(di-(1-6C) alkyl), CH=CH or C(1-6C alkyl)=CH;

R5+R'6 and R5+R'7 = CH=CH or CH=C(1-6C alkyl);

a, b, u, v, t, r', n, a and b = 0 - 3;

M = O, S, S(O) or S(O)2;

X', Y' and Z' = CH2, CH(1-6C alkyl) or C(di-(1-6C) alkyl);

R10 and R12 = OR14, O(CO)R14, O(CO)OR16 or O(CO)NR14R15;

R11 and R13 = H, 1-6C alkyl or aryl;

R10+R11 and R12+R13 = =O;

R2 = aryl, benzyl, benzyloxy or aryloxy (all mono- to tri-substituted by

R17), H, 1-10C alkyl, 2-10C alkenyl, 2-10C alkynyl, 3-6C cycloalkyl, 3-6C cycloalkenyl, halogen, NR14R15, NR14R15(1-6C alkylene), NR14R15C(O)(1-6C alkylene), NHC(O)R16, OH, 1-6C alkoxy, -OC(O)R16, COR14, hydroxy(1-6C) alkyl, 1-6C alkoxy-1-6C alkyl, NO2, S(O)0-2R16, SO2NR14R15, 1-6C alkylene-COOR14, =O, (1,3)dioxolane, (1,3)dioxane, 1-6C alkyl, aryl, aryloxy, 1-6C alkylcarbonyl, arylcarbonyl, -(CH2)1-6-CON18R18, OH, a group of formula (Ib) or (Ic);
J = O, NH, NR18 or CH2;
R3 and R4 = 1-6C alkyl, -OR14, , -O(CO)R14, -O(CO)OR16, -O(CH2)1-5OR14, -O(CO)NR14R15, -NR14R15, -NR14(CO)R15, -NR14(CO)OR16, -NR14(CO)NR15R19, -NR14SO2R16, -COOR14, -CONR14R15, -COR14, -SO2NR14R15, S(O)0-2R16, -O(CH2)1-10-COOR14, -O(CH2)1-10CONR14R15, -(1-6C alkylene)-COOR14, -CH=CH-COOR14, -CF3, -CN, -NO2 or halo;
R'8 = H, 1-6c alkyl, aryl(1-6C)alkyl, -C(O)R14 or -COOR14;
R'9 and R17 = H, 1-6C alkyl, 1-6C alkoxy, -COOH, NO2, -NR14R15, OH or halo;
R14 and R15 = H, 1-6C alkyl (optionally substituted by aryl) or aryl;
R16 = 1-6C alkyl or aryl (optionally mono- to tri-substituted by R17);
R18 = H or 1-6C alkyl;
R19 = H, OH or 1-6C alkoxy;
Ar'1 = aryl (optionally mono- to penta-substituted by R'10 or heteroaryl;
Ar'2 = aryl (optionally mono- to penta-substituted by R'4);
Ar'3 = aryl (optionally mono- to penta-substituted by R'5);
R+R1 = =O;
r and p' = 0 - 2;
R'4 = T', lower alkyl;
T' = T, -O(CH2)1-5OR6, -NR6SO2R9, S(O)0-2R9 or -O(CH2)1-10-COOR6;
R'5 = T', -CF3, -CN, -NO2 or halo;
R'10 = T' (except -(lower alkylene)COOR6 or -CH=CH-COOR6), -CF3, -CN, -NO2 or halo;
R1 = CH, C(lower alkyl), CF, C(OH), C(C6H5), C(C6H4-R15), N or N+O-;
R2 and R3 = CH2, CH(lower alkyl), C(di-lower alkyl), CH=CH or C(lower alkyl)=CH;
R1+R2 or R1+R3 = CH=CH or CH=C(lower alkyl);
R4 = B-(CH2)m', B-(CH2)q, B-(CH2)e-Z-(CH2)r', B-(2-6C alkenylene)-, B(4-6C alkadienylene), B-(CH2)t-Z-(2-6C alkenylene), B-(CH2)f-V-(CH2)g, B-(CH2)t-V-(2-6C alkenylene), B-(2-6C alkenylene)-V-(CH2)t, B-(CH2)a'-Z-(CH2)b'-V-(CH2)d' or T-(CH2)s';
T = 3-6C cycloalkyl;
R1+R4 = (B-CH=C-);
B = pyrrolyl, pyridinyl, pyrimidinyl, pyrazinyl, triazinyl, imidazolyl, thiazolyl, pyrazolyl, thienyl, oxazolyl, furanyl, nitrogen containing heteroaryls or their N-oxide (all optionally mono- to tri-substituted by W), indanyl, indenyl, naphthyl, tetrahydronaphthyl or phenyl (substituted by R15a, R16a or R17a);
W = benzyl, benzyloxy, phenoxy, dioxolanyl (all optionally mono- to tri-substituted by R7), lower alkyl, hydroxy lower alkyl, lower alkoxy, alkoxyalkyl, alkoxyalkoxy, alkoxycarbonylalkoxy, (lower alkoxyimino)-lower alkyl, lower alkanedioyl, lower alkyl lower alkanedioyl, allyloxy, CF3, OCF3, NO2, N(R8a)(R9a), N(R8a)(R9a)-lower alkylene, N(R8a)(R9a)-lower alkylenyloxy, OH, halo, CN, N3, NHC(O)OR10, NHC(O)R10, R11O2SNH-, (R11O2S)2N, S(O)2NH2, S(O)0-2R8a, tert-butyldimethyl-silyloxymethyl, C(O)R12, COOR19, CON(R8a)(R9a), CH=CHC(O)R12, lower alkylene-C(O)R12, R10C(O)(lower alkylenyloxy), N(R8a)(R9a)C(O)(lower alkylenyloxy) or a group of formula (Id) (substituted by lower alkyl, lower alkoxy, C(O)OR10, C(O)R10, OH, N(R8a)(R9a)-lower alkylene, N(R8)(R9)-lower alkylenyloxy, S(O)2NH2 or 2-(trimethylsilyl)-ethoxymethyl;
R7 = lower alkyl, lower alkoxy, -COOH, NO2, -N(R8)(R9), OH or halo;
R8a and R9a = H or lower alkyl;
R10 = phenyl or benzyl (both optionally mono to trisubstituted by R7) or lower alkyl;
R11 = phenyl or benzyl (both optionally mono to trisubstituted by R7), OH or lower alkyl;
R12 = H, OH, alkoxy, phenoxy, benzyloxy, a group of formula (Ie), -N(R8a)(R9a), lower alkyl or phenyl (optionally mono- to tri-substituted by R7);
R13 = O, CH2, NH, N(lower alkyl) or NC(O)R19;
R15a, R16a and R17a = H or W;
R16a+R17a = dioxolanyl ring;
R19 = H, lower alkyl, phenyl or phenyl lower alkyl;
R20 and R2 = phenyl, naphthyl, heteroaryl, benzofused heteroaryl (all optionally substituted by W), indanyl, indenyl, tetrahydronaphthyl, benzodioxolyl, or cyclopropyl;
A = CH=CH-, -CC- or -(CH2)p'-;
B' = phenyl (substituted by R'1, R'2 and R'3);
B = phenyl (substituted by R'1', R'2' and R'3');

D = (CH2)mC(O)- or -(CH2)q'-;
m = 1 - 4;
q' = 2 - 4;
E = 10-20C alkyl or -C(O)(9-19C) alkyl;
R' = H, 1-15C alkyl or B-(CH2)r'-;
R'1 - R'3 and R'1' - R'3' = H, lower alkyl, lower alkoxy, carboxy, NO2, NH2, OH, halo, lower alkylamino, dilower alkylamino, NHC(O)OR'5, R'6O2SNH- or -S(O)2NH2;
R'4 = phenyl (substituted by (OR'5)n);
R'5 = lower alkyl;
R'6 = OH, lower alkyl, phenyl (optionally mono- to tri-substituted by lower alkyl, lower alkoxy, carboxy, NO2, NH2, OH, halo, lower alkylamino or di-lower alkylamino) or benzyl;
R26 = H or OG1;
G and G1 = a group of formula (If), (Ig), (Ih) or (Ii);
R, Ra and Rb = H, OH, halo, -NH2, azido, (1-6C)alkoxy(1-6C)alkoxy or W'-R30;
W' = NH-C(O), O-C(O), O-C(O)-N(R31), NH-C(O)-N(R31) or O-C(S)-N(R31);
R2 and R6 = H, 1-6C alkyl, aryl or aryl(1-6C) alkyl;
R3, R4, R5, R7, R3a or R4a = H, 1-6C alkyl, aryl(1-6C)alkyl, -C(O)(1-6C)alkyl or -C(O)aryl;
R30 = T', T'-(1-6C)alkyl, (2-4C)alkenyl, (1-6C)alkyl, (3-7C)cycloalkyl or (3-7C)cycloalkyl(1-6C)alkyl (all substituted by R32);
R31 = H or 1-4C alkyl;
T' = phenyl, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, benzothiazolyl, thiadiazolyl, pyrazolyl, imidazolyl or pyridyl;
R32 = halo, 1-4C alkyl, OH, phenoxy, CF3, NO2, 1-4C alkoxy, methylenedioxy, oxo, 1-4C alkylsulfanyl, 1-4C alkylsulfinyl, 1-4C alkylsulfonyl, N(CH3)2, C(O)-NH(1-4C)alkyl, C(O)-N((1-4C)alkyl)2, C(O)-(1-4C)alkyl, C(O)(1-4C)alkoxy, pyrrolidinylcarbonyl or covalent bond;
NR31R32 = pyrrolidinyl, piperidinyl, N-methyl-piperazinyl, indolinyl or morpholinyl (all optionally substituted by 1-4C alkoxycarbonyl);
Ar1 = aryl (optionally mono- to tri-substituted by R'10) or A3;
A3 = pyridyl, isoxazolyl, furanyl, pyrrolyl, thienyl, imidazolyl, pyrazolyl, thiazolyl, pyrazinyl, pyrimidinyl or pyridazinyl;
Ar2 = aryl (optionally mono- to tri-substituted by R'11);
Q' = a bond or a group of formula (Ij);
R1 = (CH2)q, (CH2)e-E'-(CH2)r', (2-6C)alkenylene, (CH2)f-V-(CH2)g or A2;
A2 = -M-Y'd-C(R'15)(R'16)-Z'h-, -X'm-(C)s(R'17)(R'18)-Y'n-(R'15)(R'16)-Z'p- or -X'j-(C)v(R'15)(R'16)-Y'k-S(O)0-2-;
E' = O, C(O),phenylene, -NR22- or -S(O)0-2-;
R'12 = CH, C(1-6C)alkyl, CF, C(OH), C(C6H4-R23), N or N+O-;
R'13 and R'14 = -CH2-, CH(1-6C alkyl)-, -C(di-(1-6C)alkyl), -CH=CH- or -C(1-6C alkyl)=CH-;
R'12+R'13 and R'12+R'14 = CH=CH or CH=C(1-6C alkyl);
R'10 and R'12 = 1-6C alkyl, OR'19, O(CO)R'19, O(CO)OR'21, O(CH2)1-5OR'19, O(CO)NR'19R'20, -NR'19R'20, NR'19(CO)R'20,NR'19(CO)OR'21, NR'19(CO)NR'20R'25, NR'19SO2R'21, COOR'19, CONR'19R'20, COR'19, SO2NR'19R'20, S(O)0-2R'21, O(CH2)1-10-COOR'19, O(CH2)1-10CONR'19R'20, (1-6C alkylene)-COOR'19, CH=CH-COOR'19, CF3, CN, NO2 or halo;
R'15 and R'17 = OR'19, O(CO)R'19, O(CO)OR'21 or O(CO)NR'19R'20;
R'16 and R'18 = H, 1-6C alkyl or aryl;
R'15+R'16 and R'17+R'18 = =O;
R'19 and R'20 = H, 1-6C alkyl (optionally substituted by aryl) or aryl;
R'21 = 1-6C alkyl or aryl (optionally mono- to tri-substituted by R'24);
R'22 = H, 1-6C alkyl, aryl(1-6C)alkyl, -C(O)R'19 or -COOR'19;
R'23 and R'24 = H, 1-6C alkyl, 1-6C alkoxy, COOH, NO2, NR'19R'20, OH or halo;
R'25 = H, OH or 1-6C alkyl;
R26 = OH, OCH3, fluorine or chlorine;
R' = (If) - (Ii), -SO3H or natural or unnatural amino acids;
R32 = H or R32;
Ar'1 = Ar1, pyridyl, isoxazolyl, furanyl, pyrrolyl, thienyl, imidazolyl, pyrazolyl, thiazolyl, pyrazinyl, pyrimidinyl or pyridazinyl;
Q = (CH2)q or (Ij).
Provided that:
(1) when U is Ar2, then U' is Ar3 and U is Zp-(C)r(R2)(R3)-Yn-(C)q(R)(R1)-Xm-Ar1;
(2) when U is Ar'2, then U' is Ar'3 and U is Zp-C(R'1)(R'2)-Yq'-A-Ar'1;
(3) when U is Ar2, then U' is phenyl (substituted by A and R19) and U is Q-R1-Ar1;
(4) when U is Ar'3, then U' is Ar'2 and U is S(O)r-Yn'-(C)q'(R)(R1)-Xm'-Ar'1;
(5) when U is Ar2, then U' is phenyl (substituted by -O-G) and at position 2 by R26) and U is Q'-R1-Ar1;
(6) when U is Ar2, then U' is phenyl (substituted by R26) and U is

Q-CH(R'1)-Ar'1;
(7) at least one of q and r is 1;
(8) when p is 0 and r is 1 then m+q+n is 1 - 5;
(9) when Q forms a spiro ring, q can also be 0 or 1;
(10) both a and b are not zero;
(11) when R'6 is -CH=CH- or -C(1-6C alkyl)=CH- then a is 1;
(12) when R'7 is -CH=CH- or -C(1-6C alkyl)=CH- then b is 1;
(13) when a is 2 or 3 then R'6 can same or different;
(14) when b is 2 or 3 then R'7 can same or different;
(15) when Q is a bond then R1 is A1;
(16) at least one of s and t is 1 and sum of m, n, p, s and t is 1 - 6;
(17) when p is 0 and t is 1 then the sum of m, s and n is 1 - 5;
(18) when p is 0 and s is 1, then sum of m, t and n is 1 - 5;
(19) when R2 is substituent on heterocycloalkyl then R2 is =O,
(1,3)dioxolane or (1,3)dioxane, where R2 is a substituent on a
substitutable ring N which is H, 1-6C alkyl, aryl, 1-6C alkoxy, aryloxy,
1-6C alkylcarbonyl, arylcarbonyl, OH, -(CH2)1-6CONR18R18, (Ib) or (Ic);
(20) both u and v are not both 0;
(21) R2 is -CH=CH- or -C(lower alkyl)=CH- then v is 1 and when R3 is
-CH=CH- or -C(lower alkyl)=CH- then u is 1;
(22) when v is 2 or 3 then R2 or R3 can be same of different;
(23) sum of t and the number of carbon in alkenylene is 2 - 6;
(24) In E and R', the alkyl is straight, branched, saturated or containing
at least one double bonds;
(25) when R26 is H or OH then G is not H;
(26) both a and b are not zero;
(27) when R'13 is -CH=CH- or -C(1-6C alkyl)- then a is 1 and when R'14 is
=CH=CH- or =C(1-6C alkyl)- then b is 1;
(28) when a or b is 2 or 3 then R'13 or R'14 can be same or different;
(29) when Q' is a bond then R1 is A2; and
(30) when Q' is a bond then R1 is -X'j-(C)v(R'15)(R'16)-Y'k, S(O)0-2- and
Ar1 is A3.
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The
composition further comprises at least one cholesterol biosynthesis
inhibitor, bile acid sequestrant, low-density lipoprotein receptor
activator, Omega 3 fatty acid, natural water soluble fiber,
antioxidant or vitamin.
Preferred Components: The blood modifier is:
(1) an anti-coagulant (argatroban, bivalirudin, daltaparin sodium,
desirudin, dicumarol, lyapolate sodium, nafamostat mesylate,
phenprocoumon, tinzaparin sodium and/or warfarin sodium);
(2) an antithrombotic agent (anagrelide hydrochloride, bivalirudin,
cilostazol, dalteparin sodium, danaparoid sodium, dazoxiben hydrochloride,
efegatran sulfate, enoxaparin sodium, fluretofen, ifetroban, ifetroban
sodium, lamifiban, lotrafiban hydrochloride, napsagatran, orbofiban
acetate, roxifiban acetate, sibrafiban, tinzaparin sodium, trifenagrel,
abciximab and/or zolimomab aritox);
(3) a fibrinogen receptor antagonist (roxifiban acetate, fradafiban,
orbofiban, lotrafiban hydrochloride, tirofiban, xemilofiban, monoclonal
antibody 7E3 and/or sibrafiban);
(4) a platelet inhibitor (cilostazol, clopidogrel bisulfate, epoprostenol,
epoprostenol sodium, ticlopidine hydrochloride, aspirin, ibuprofen,
naproxen, sulindae, idomethacin, mefenamate, droxicam, diclofenac,
sulfinpyrazone, piroxicam and/or dipyridamole (preferably aspirin));
(5) a platelet aggregation inhibitor (acadesine, beraprost, beraprost
sodium, ciprostene calcium, itazigrel, lifarizine, lotrafiban
hydrochloride, orbofiban acetate, oxagrelate, fradafiban, orbofiban,
tirofiban and/or xemilofiban);
(6) a hemorrheologic agent (pentoxifylline);
(7) a lipoprotein associated coagulation inhibitor;
(8) a Factor VIIa inhibitor (4H-3,1-benzoxazin-4-one, 4H-3,1-benzoxazin-4-
thione, quinazolin-4-one, quinazolin-4-thione, benzothiazin-4-one,
imidazolyl-boronic acid-derived peptide analogue TFPI-derived peptide,
naphthalene-2-sulfonic acid (1-(3-(aminoiminomethyl)-benzyl)-2-oxo-
pyrrolidin-3-(S)-yl) amide trifluoroacetate, dibenzofuran-2-sulfonic acid
(1-(3-(aminomethyl)-benzyl)-5-oxo-pyrrolidin-3-yl)-amide,
toluene-4-sulfonic acid (1-(3-(aminoiminomethyl)-benzyl)-2-oxo-pyrrolidin-
3-(S)-yl)-amide trifluoroacetate and/or 3,4-dihydro-1H-isoquinoline-2-
sulfonic acid (1-(3-(aminoiminomethyl)-benzyl)-2-oxo-pyrrolin-3-(S)-yl)-
amide trifluoro acetate);
(9) a Factor Xa inhibitor (disubstituted pyrazolines, disubstituted
triazolines, substituted n-((aminoiminomethyl)phenyl)propylamides,
substituted n-((aminomethyl)phenyl)propylamides, ***tissue***
factor ***pathway*** ***inhibitor*** (TFPI), low molecular
weight heparins, heparinoids, benzimidazolines, benzoxazolinones,
benzopiperazinones, indanones, dibasic (amidinoaryl)propanoic acid
derivatives, amidinophenyl-pyrrolidines, amidinophenyl-pyrrolines,

amidinophenyl-isoxazolidines, amidinoindoles, amidinoazoles, bis-arylsulfonylaminobenzamide derivatives and/or peptidic Factor Xa inhibitor);
(10) a low molecular weight heparin (enoxaparin, nardroparin, dalteparin, certroparin, parnaparin, reviparin and/or tinzaparin); and/or
(11) a heparinoid (danaparoid).
The cholesterol biosynthesis inhibitor comprises at least one HMG CoA reductase inhibitor. The HMG-CoA reductase inhibitor is simvastatin.

L7 ANSWER 21 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-471618 [50] WPIDS
DNC C2002-134165
TI Identifying arterial smooth muscle cells in (a tissue sample from) a mammal, useful for targeting arterial or venous cells individually for e.g. therapy, comprises detecting an indicator gene of the Ephrin B2 or the expression of Ephrin B2.
DC B04 D16
IN ANDERSON, D J; GARCIA-CARDENA, G; GIMBRONE, M A; WANG, H U
PA (BGHM) BRIGHAM & WOMENS HOSPITAL INC; (CALY) CALIFORNIA INST OF TECHNOLOGY
CYC 100
WO 2002040540 A2 20020523 (200250)* EN 82<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
A 2002032405 A 20020527 (200261) <--
U 2002136726 A1 20020926 (200265) <--
E 1337276 A2 20030827 (200357) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT W 2002040540 A2 WO 2001-US42961 20011120; AU 2002032405 A AU 2002-32405 2 1120; US 2002136726 A1 Provisional US 2000-252009P 20001120, US -988496 20011120; EP 1337276 A2 EP 2001-991925 20011120, WO -US42961 20011120
FDT A 2002032405 A Based on WO 2002040540; EP 1337276 A2 Based on WO 040540
PRAI US 2000-252009P 20001120; US 2001-988496 20011120
-471618 [50] WPIDS
00240540 A UPAB: 20020807
LTY - Identifying arterial smooth muscle cells in a transgenic animal n a tissue sample from a mammal comprising detecting the expression of ndicator gene inserted in one or more alleles of Ephrin B2 or by cting the expression of the Ephrin B2 transmembrane ligand, is new.
DETAILED DESCRIPTION - Identifying arterial smooth muscle cells in a sgenic animal, where the genome of the animal comprises a recombinant eic acid encoding an indicator gene inserted in one or more alleles of hropoietin-producing human hepatocellular carcinoma cell receptor rin) B2, comprising:
(a) detecting expression of the indicator gene; and
(b) detecting expression of a smooth muscle cell-specific protein; cells that express both the indicator gene and the smooth muscle cell-specific protein are arterial smooth muscle cells, is new.
Identifying an arterial smooth muscle cell in a tissue sample from a mammal comprising:
(a) contacting the tissue sample with a first composition that binds to Ephrin B2;
(b) contacting the tissue sample with a second composition that binds to a protein that is expressed on smooth muscle cells; and
(c) detecting expression of the first and second compositions, where of the first and second compositions are co-expressed on a cell, the cell is an arterial smooth muscle cell, is new.
INDEPENDENT CLAIMS are also included for the following:
(1) selectively delivering an agent to arterial smooth muscle cells in a mammal by administering to the mammal a composition comprising:
(a) the agent; and
(b) a substance that selectively binds an arterial smooth muscle cell-specific surface molecule (i.e. an Ephrin family ligand or an Eph family receptor);
(2) a transgenic animal whose genome comprises a recombinant nucleic acid encoding an indicator gene, which is expressed in arterial smooth muscle cells but is not detectably expressed in venous smooth muscle cells;
(3) assessing an effect of an agent in arterial smooth muscle cells;
(4) isolating arterial smooth muscle cells;
(5) arterial smooth muscle cells isolated using the method of (4);

(6) a cell line derived from the arterial smooth muscle cells of (5);
(7) a cDNA produced from the isolated arterial smooth muscle cells of (5);
(8) an oligonucleotide encoding a targeting molecule comprising:
(a) a first nucleic acid sequence comprising a promoter region of Ephrin B; and
(b) a second nucleic acid sequence encoding a polypeptide, where the first nucleic acid sequence is operably linked to the second nucleic acid sequence;
(9) inducing the expression of a polypeptide in arterial smooth muscle cells of a mammal by administering the targeting molecule cited in (8);
(10) modifying arteries in a mammal;
(11) modulating or altering angiogenesis in a mammal;
(12) an artificially prepared vessel comprising arterial smooth muscle cells that comprise a recombinant nucleic acid, which increases the expression of ephrin B2 above endogenous levels; and
(13) diagnosing the presence of a tumor by detecting the expression of Ephrin B2 in blood vessels from a mammal and comparing the expression with a control.

ACTIVITY - Angiogenic; Antiangiogenic; Thrombolytic; Vasotropic; Antiatherosclerotic; Cytostatic; Vulnerary. No supporting data is given in the source material.

MECHANISM OF ACTION - Gene therapy.

USE - The method is useful for distinguishing arterial from venous cells. The method is particularly useful for identifying arterial smooth muscle cells in a transgenic animal or in a tissue sample from a mammal. This allows arteries and arterial cells, as well as veins and venous cells, to be targeted, manipulated or processed individually or separately for research, diagnostic and/or therapeutic purposes. Specifically, the method is useful for targeting arterial cells for modulating or altering angiogenesis in a mammal (claimed).

Dwg.0/4

PI WO 2002040540 A2 20020523 (200250)* EN 82 C07K014-705 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
AU 2002032405 A 20020527 (200261) C07K014-705 <--
US 2002136726 A1 20020926 (200265) A61K039-395 <--
EP 1337276 A2 20030827 (200357) EN A61K048-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

ADT WO 2002040540 A2 WO 2001-US42961 20011120; AU 2002032405 A AU 2002-32405 20011120; US 2002136726 A1 Provisional US 2000-252009P 20001120, US 2001-988496 20011120; EP 1337276 A2 EP 2001-991925 20011120, WO 2001-US42961 20011120

FDT AU 2002032405 A Based on WO 2002040540; EP 1337276 A2 Based on WO 2002040540

PRAI US 2000-252009P 20001120; US 2001-988496 20011120

TECH UPTX: 20020807

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Detecting the expression of the indicator gene comprises staining a tissue sample from the transgenic animal with a substance appropriate for the detection of the expression of the indicator gene. The indicator gene is an Ephrin family ligand gene. The smooth muscle cell-specific protein is smooth muscle actin, which is detected using an antibody or its antigen-binding fragment. In the method, the both the first and second compositions are selected from the antibody or its antigen-binding fragment. Preferably, the second composition is an antibody or antigen-binding fragment that binds smooth muscle actin. A label (e.g. a fluorescent label, a colorimetric label, an enzyme label, an affinity label, an epitope label, a spin label or a chemiluminescent group) is conjugated to the first and second compositions. The arterial smooth muscle cell-specific surface molecule is an Ephrin family ligand, specifically Ephrin B2. The substance or composition is an antibody or its antigen-binding fragment which binds to Ephrin B2 or to the extracellular domain of Ephrin B2. The agent is an angiogenic agent or an anti-angiogenic agent. The agent inhibits conditions selected from thrombosis, stenosis, restenosis or formation of atherosclerotic plaques. Specifically, the agent is a cyclin G1 mutant polypeptide, a p27-p16 chimeric polypeptide, a hepatocyte growth factor, a herpes simplex virus thymidine kinase polypeptide, a cytosine deaminase-5-flurocytosine polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative

H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, a synthetic double-stranded nucleic acid with high binding affinity for E2F, an antisense oligonucleotide to p65, an antisense oligonucleotide to basic fibroblast growth factor, an active site inactivated factor VIIa polypeptide, a recombinant ***tissue*** ***factor*** ***pathway*** ***inhibitor*** , rapamycin, an ***antioxidant*** , a glycoprotein IIb/IIIa receptor antagonist, a calcium channel blocker or a nitric oxide donor. The agent is conjugated to the substance. In method (3), assessing an effect of an agent on arterial smooth muscle cells comprises:
(a) administering the agent to a transgenic animal whose genome comprises a recombinant nucleic acid encoding the indicator gene inserted in one or more alleles of Ephrin B2;
(b) observing the effect of the agent by detecting the expression of the indicator gene; and
(c) comparing it to a control.
The agent modulates, preferably inhibits, the proliferation of arterial smooth muscle cells. The method may also comprise assessing an effect of an agent on the arterial smooth muscle cells isolated in method (4) by:
(a) adding the agent to the isolated arterial smooth muscle cells; and
(b) comparing the effect of the agent on the isolated arterial smooth muscle cells with a control, which comprises arterial smooth muscle cells in the absence of the agent.
In method (4), isolating arterial smooth muscle cells comprises:
(a) dissociating cells of a tissue sample comprising arterial smooth muscle cells;
(b) contacting the dissociated cells with a first substance that binds to a cell-surface protein (i.e. an Ephrin family ligand or an Eph family receptor) expressed on arterial smooth muscle cells;
(c) contacting the dissociated cells with a second substance that binds to a cell-surface protein expressed on smooth muscle cells; and
(d) separating those cells which have bound both the first and second substances from those cells which have not bound to the first and second substances.
Those that bind both the first and second substances are arterial smooth muscle cells. In particular, the cell-surface protein expressed on arterial smooth muscle cells is an Ephrin family ligand. In method (9), the targeting molecule is administered by retroviral gene delivery, adenoviral gene delivery or naked DNA injection. The targeting molecule is administered using a gene gun, cationic liposomes, molecular conjugates or a catheter. In method (10), arteries in a mammal are modified by:
(a) isolating arterial smooth muscle cells;
(b) introducing the targeting molecule into the isolated arterial smooth muscle cells; and
(c) introducing the arterial smooth muscle cells, which comprise the targeting molecule, into the mammal.
Modulating angiogenesis in a mamma comprises administering a composition comprising:
(a) an agent; and
(b) a substance that binds an arterial smooth muscle cell-specific surface molecule, specifically Ephrin, so that the substance binds to the arterial smooth muscle cell-specific surface molecule.
The method may also comprise administering the targeting molecule to the mammal. Altering angiogenesis in a mammal comprises administering a composition which binds Ephrin B2 expressed on arterial smooth muscle cells. Angiogenesis is either inhibited or promoted. In particular, angiogenesis occurs in tumor growth or wound healing.
Preferred Oligonucleotide: The second nucleic acid sequence encodes a polypeptide that is a protein or its functional fragment. In particular, the second nucleic acid encodes a polypeptide consisting of herpes simplex virus thymidine kinase polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a cyclin-dependent kinase inhibitor polypeptide, a mutant cyclin G1 polypeptide, a nitric oxide synthase (NOS) polypeptide, a growth arrest homeobox, vascular cyclo-oxygenase polypeptide, a thrombomodulin polypeptide, a vascular endothelial growth factor, a chimeric p27-p16 polypeptide, a hepatocyte growth factor, a cytosine deaminase-5-flurocytosine polypeptide, a chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS polypeptide, an iNOS polypeptide, an active site inactivated factor VIIa polypeptide or a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** polypeptide.
Preferred Animal: The transgenic animal is a mammal. Preferably, the mammal is a mouse, rat, guinea pig, pig, rabbit or sheep.

L7 ANSWER 22 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-257208 [30] WPIDS
CR 2002-226957 [28]

DNN N2002-199142 DNC C2002-076497
TI Managing anticoagulation therapy in a patient involves administering acute phase anticoagulant during acute phase of coagulation and active-site inhibited factor VIIa polypeptide during chronic phase of coagulation.
DC A96 B04 S03
IN NELSESTUEN, G L
PA (MINU) UNIV MINNESOTA; (NELS-I) NELSESTUEN G L
CYC 96
PI WO 2002003075 A2 20020110 (200230)* EN 90<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001070171 A 20020114 (200237) <--
US 2003211460 A1 20031113 (200382)
ADT WO 2002003075 A2 WO 2001-US20307 20010626; AU 2001070171 A AU 2001-70171 20010626; US 2003211460 A1 WO 2001-US20307 20010626, US 2002-312685 20021230
FDT AU 2001070171 A Based on WO 2002003075
PRAI US 2000-607716 20000630; US 2002-312685 20021230
AN 2002-257208 [30] WPIDS
CR 2002-226957 [28]
AB WO 200203075 A UPAB: 20031223
NOVELTY - Managing (I) anticoagulation therapy in a patient comprises administering an acute phase anticoagulant to the patient during the acute phase of coagulation, and administering a chronic phase anticoagulant to the patient during the chronic phase of coagulation.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) evaluating (II) patient responsiveness to factor VIIa or activated protein C (APC) therapy by adding factor VIIa or APC to whole blood sample and monitoring activated clotting time (ACT) of blood sample in absence of added phospholipid, where significant decrease in ACT compared to control sample from patient in the absence of added factor VIIa or APC indicates that patient is responsive to factor VIIa or APC;

(2) detecting (III) tissue factor in blood, by obtaining an anticoagulated blood sample, neutralizing factor VIII or IX and neutralizing tissue factor in the anticoagulated blood sample and assaying ACT of the anticoagulated blood sample in the presence of added factor VIIa, where the presence or absence of tissue factor is detected by comparing ACT of the anticoagulated blood sample relative to a corresponding anticoagulated blood sample without neutralized tissue factor;

(3) evaluating (IV) dosage of APC, by obtaining a whole blood sample from a patient undergoing APC therapy, and monitoring ACT of the whole blood sample in the absence of added phospholipid, where a significant increase in ACT compared to a control sample from the patient before APC therapy indicates that an appropriate dosage of APC has been administered;

(4) a kit (V) for detecting tissue factor, comprising anti-factor VIII or anti-factor IX antibody, an anticoagulant and factor VIIa; and

(5) a kit (VI) for detecting factor VIIa or APC in blood, comprising a Ca2+ ***chelator*** , a calcium salt and an activator of contact phase of coagulation.

ACTIVITY - Thrombolytic; Anticoagulant.
No supporting data is given.
MECHANISM OF ACTION - Regulator of coagulation.
USE - (I) is useful for managing anticoagulation therapy. (II) is useful for monitoring patient responsiveness to factor VIIa or APC. The assays provides the ability to detect genetic disorders such as APC resistance or protein S deficiency. (III) is useful to screen or diagnose coagulation disorders that result in altered tissue factor expression in the circulation e.g. arteriosclerosis or cancer. (IV) is useful for evaluating the dosage of APC.

ADVANTAGE - Modifications to vitamin K-dependent polypeptides increase their circulation half-life and their activity, and also reduce the amount of protein needed to treat clotting disorders as well as decrease the frequency of the administration. The method allows individual patients to be monitored such that therapies can be tailored, minimizing costs associated with such therapies. The methods have excellent reproducibility.
Dwg.2A/16
PI WO 2002003075 A2 20020110 (200230)* EN 90 G01N033-86 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001070171 A 20020114 (200237) G01N033-86 <--
US 2003211460 A1 20031113 (200382) C12Q001-00

ADT WO 2002003075 A2 WO 2001-US20307 20010626; AU 2001070171 A AU 2001-70171 20010626; US 2003211460 A1 WO 2001-US20307 20010626, US 2002-312685 20021230

FDT AU 2001070171 A Based on WO 2002003075

PRAI US 2000-607716 20000630; US 2002-312685 20021230

AB WO 200203075 A UPAB: 20031223

NOVELTY - Managing (I) anticoagulation therapy in a patient comprises administering an acute phase anticoagulant to the patient during the acute phase of coagulation, and administering a chronic phase anticoagulant to the patient during the chronic phase of coagulation.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) evaluating (II) patient responsiveness to factor VIIa or activated protein C (APC) therapy by adding factor VIIa or APC to whole blood sample and monitoring activated clotting time (ACT) of blood sample in absence of added phospholipid, where significant decrease in ACT compared to control sample from patient in the absence of added factor VIIa or APC indicates that patient is responsive to factor VIIa or APC;

(2) detecting (III) tissue factor in blood, by obtaining an anticoagulated blood sample, neutralizing factor VIII or IX and neutralizing tissue factor in the anticoagulated blood sample and assaying ACT of the anticoagulated blood sample in the presence of added factor VIIa, where the presence or absence of tissue factor is detected by comparing ACT of the anticoagulated blood sample relative to a corresponding anticoagulated blood sample without neutralized tissue factor;

(3) evaluating (IV) dosage of APC, by obtaining a whole blood sample from a patient undergoing APC therapy, and monitoring ACT of the whole blood sample in the absence of added phospholipid, where a significant increase in ACT compared to a control sample from the patient before APC therapy indicates that an appropriate dosage of APC has been administered;

(4) a kit (V) for detecting tissue factor, comprising anti-factor VIII or anti-factor IX antibody, an anticoagulant and factor VIIa; and

(5) a kit (VI) for detecting factor VIIa or APC in blood, comprising a Ca2+ ***chelator*** , a calcium salt and an activator of contact phase of coagulation.

ACTIVITY - Thrombolytic; Anticoagulant.

No supporting data is given.

MECHANISM OF ACTION - Regulator of coagulation.

USE - (I) is useful for managing anticoagulation therapy. (II) is useful for monitoring patient responsiveness to factor VIIa or APC. The assays provides the ability to detect genetic disorders such as APC resistance or protein S deficiency. (III) is useful to screen or diagnose coagulation disorders that result in altered tissue factor expression in the circulation e.g. arteriosclerosis or cancer. (IV) is useful for evaluating the dosage of APC.

ADVANTAGE - Modifications to vitamin K-dependent polypeptides increase their circulation half-life and their activity, and also reduce the amount of protein needed to treat clotting disorders as well as decrease the frequency of the administration. The method allows individual patients to be monitored such that therapies can be tailored, minimizing costs associated with such therapies. The methods have excellent reproducibility.

Dwg.2A/16

TECH UPTX: 20020513

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (I), the acute phase is during surgery and the acute phase anticoagulant is heparin. The chronic phase anticoagulant is an active-site inhibited factor VIIa polypeptide linked to a PEG polymer, an antibody having specific binding affinity for tissue factor, or a ***tissue*** ***factor*** ***pathway*** ***inhibitor*** . In (II), ACT is monitored in a device which comprises an activator of the contact phase of coagulation. In (IV), the clotting time is measured in the presence of an activator of the contact phase of coagulation.

Preferred Kit: In (V), the anticoagulant is a Ca2+ ***chelator*** , preferably citrate or oxalate and (V) further comprises a calcium salt. (VI) further comprises factor VIIa and APC.

L7 ANSWER 23 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2001-638822 [73] WPIDS

CR 2001-529690 [49]; 2001-549911 [49]; 2001-549912 [49]; 2001-549918 [49]; 2001-557518 [49]

DNN N2001-477536 DNC C2001-188891
TI Preventing or reducing intimal hyperplasia at insults to internal structures of patients by contacting exterior surface with drug delivery vehicle comprising intimal hyperplasia preventing agent.
DC A96 B05 B07 P34
IN CUNANAN, C M; HELMUS, M N; TREMBLE, P; CUNANAN, C
PA (EDWA-N) EDWARDS LIFESCIENCES CORP; (CUNA-I) CUNANAN C M; (HELM-I) HELMUS M N; (TREM-I) TREMBLE P
CYC 95
PI WO 2001054748 A1 20010802 (200173)* EN 56<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001032999 A 20010807 (200174) <--
US 2002026236 A1 20020228 (200220) <--
EP 1250166 A1 20021023 (200277) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003520830 W 20030708 (200347) 69
US 6730313 B2 20040504 (200430)
ADT WO 2001054748 A1 WO 2001-US2563 20010125; AU 2001032999 A AU 2001-32999 20010125; US 2002026236 A1 Provisional US 2000-178087P 20000125, US 2001-771480 20010125; EP 1250166 A1 EP 2001-905081 20010125, WO 2001-US2563 20010125; JP 2003520830 W JP 2001-554731 20010125, WO 2001-US2563 20010125; US 6730313 B2 Provisional US 2000-178087P 20000125, US 2001-771480 20010125
FDT AU 2001032999 A Based on WO 2001054748; EP 1250166 A1 Based on WO 2001054748; JP 2003520830 W Based on WO 2001054748
PRAI US 2000-178087P 20000125; US 2001-771480 20010125
AN 2001-638822 [73] WPIDS
CR 2001-529690 [49]; 2001-549911 [49]; 2001-549912 [49]; 2001-549918 [49]; 2001-557518 [49]
AB WO 2001054748 A UPAB: 20011211
NOVELTY - Methods of preventing or reducing intimal hyperplasia at sites of insult to an internal structure of a patient comprise contacting an exterior surface of the structure contiguous with the site of insult with a drug delivery vehicle that flows during application, adheres to the exterior surface and releases intimal hyperplasia preventing agent in a time-dependent manner.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for:
(1) heart valves comprising a 1st population of bioactive material and a 2nd bioactive material with a 2nd release rate from the heart valve; and

(2) a kit comprising a bioadhesive drug delivery vehicle comprising a biologically active agent to prevent or reduce intimal hyperplasia and a set of instructions explaining the use of the drug delivery vehicle.

ACTIVITY - Cytostatic; antithrombotic; antiinflammatory; ***antioxidant*** ; anticoagulant; immunosuppressive.

Young adult dogs (10 male, 2 female) were anaesthetized, heparinized and anticoagulated (at the surgeon's discretion) before the carotid artery was cross-clamped and an interpositional graft with end-to-side anastamoses of the femoral vein to the carotid artery was performed. Test and control articles were applied to a uniform thickness and allowed to harden. Grafts were placed in both carotid arteries by serial procedures. Balloon injury to the femoral arteries by three sequences of inflation and removal of a 4 French Fogarty catheter generated 5-cm lesions in each femoral artery that were or were not treated with test/control articles. The insertion site was repaired and the animal was closed. Post-operative care was performed by known methods along with prophylactic administration of antibiotics. For 7 days after surgery, animals received 250 mg/day aspirin. The wound site was debrided and temperature, heart rate and respiratory rates were monitored daily for 1 week following surgery. Angiography of the carotid sites was performed after surgery and monthly. Intravascular ultrasound (IVUS) was used to examine the vein grafts in 10 animals at the 12-week endpoint of the study. At the end of the experiments, the overall health was monitored, including routine blood work. Animals were anticoagulated and angiography and IVUS measurements of treated vessels were taken. Animals were anaesthetized and euthanized by known methods, the carotid arteries were exposed and the healing response was evaluated. The grafts, including anastamoses, were fixed under pressure in situ and were removed along with 4 cm of proximal and distal host vessel. Femoral arteries were exposed and the healing response observed. The femoral arteries were fixed under pressure and removed with distal and proximal host tissue. Femoral and carotid arteries were stored

in 10 % neutral-buffered formalin until histology. The animals were assigned to test groups receiving:

(1) no treatment (control);
(2) fibrin vehicle;
(3) fibrin vehicle plus or minus micellar paclitaxel; and
(4) fibrin vehicle plus or minus microsphere paclitaxel.

In control animals, subcutaneous hematomas that resolved with time were observed in the carotid (1/3) and femoral (1/3) sites. Subcutaneous hematomas at the carotid site were also observed in animals treated with vehicle (2/3) and vehicle + paclitaxel (4/8)-these lesions resolved with time. A hematoma at the femoral site that reduced in size with time and healed well was present in 2/8 animals treated with paclitaxel. Two animals receiving the paclitaxel microcapsules were sacrificed before termination of the experiment because of uncontrolled bleeding at femoral and carotid sites, swellings at the left carotid area and altered mental status. Angiography showed that all carotid grafts were patent at the end of surgery and that the carotid grafts of surviving animals were patent at study end (12 weeks). Angiography at study end showed that both femoral arteries in 8/10 animals were patent; 2 appeared to be occluded at 12 weeks. IVUS showed patent vessels with some suggestion of intimal thickening in some samples. Paclitaxel limited stenosis at the proximal (P=0.08) and distal (P=0.09) anastomotic sites as assessed by angography at 12 weeks. For the carotid grafts, analysis of individual treatment groups showed that the fibrin vehicle alone also limited stenosis at the anastamotic sites, with healing in the vehicle and treated groups appearing to be similar. For the femoral grafts, angiography showed there was no significant difference between control, vehicle and paclitaxel treatment groups. Formulations containing paclitaxel had a 44 % larger lumen width (P at most 0.06) in the absence of changes in the intimal:medial ratio.

MECHANISM OF ACTION - Calcium channel blocker; converting enzyme inhibitor; cytokine inhibitor; growth factor inhibitor; growth factor sequestrant; fibrosis inhibitor; ***tissue*** ***factor*** ***inhibitor*** ; smooth muscle inhibitor; superoxide dismutase mimic; collagen synthesis inhibitor.

USE - The methods are used to prevent or reduce intimal hyperplasia, such as in vascular, intestinal and/or urinary systems (claimed) as well as organs such as the stomach, liver and intestines. They are used to prevent or reduce intimal hyperplasia at sites of insult, such as surgical insult including anastomoses following angioplasty, vascular reconstructive surgery, heart valve replacement and/or heart transplantation or in which a prosthesis (stent, graft and/or valve) is placed at the site of insult on the internal structure (claimed).

ADVANTAGE - The method is flexible enough to allow agents to be applied prior to or reapplied after surgery.

Dwg.0/0

PI WO 2001054748 A1 20010802 (200173)* EN 56 A61L031-16 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001032999 A 20010807 (200174) <--
US 2002026236 A1 20020228 (200220) A61F002-06 <--
EP 1250166 A1 20021023 (200277) EN A61L031-16 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003520830 W 20030708 (200347) 69 A61K009-06
US 6730313 B2 20040504 (200430) A61F002-02

ADT WO 2001054748 A1 WO 2001-US2563 20010125; AU 2001032999 A AU 2001-32999 20010125; US 2002026236 A1 Provisional US 2000-178087P 20000125, US 2001-771480 20010125; EP 1250166 A1 EP 2001-905081 20010125, WO 2001-US2563 20010125; JP 2003520830 W JP 2001-554731 20010125, WO 2001-US2563 20010125; US 6730313 B2 Provisional US 2000-178087P 20000125, US 2001-771480 20010125

FDT AU 2001032999 A Based on WO 2001054748; EP 1250166 A1 Based on WO 2001054748; JP 2003520830 W Based on WO 2001054748

PRAI US 2000-178087P 20000125; US 2001-771480 20010125

AB WO 200154748 A UPAB: 20011211

NOVELTY - Methods of preventing or reducing intimal hyperplasia at sites of insult to an internal structure of a patient comprise contacting an exterior surface of the structure contiguous with the site of insult with a drug delivery vehicle that flows during application, adheres to the exterior surface and releases intimal hyperplasia preventing agent in a time-dependent manner.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for:

(1) heart valves comprising a 1st population of bioactive material and a 2nd bioactive material with a 2nd release rate from the heart valve; and

(2) a kit comprising a bioadhesive drug delivery vehicle comprising a biologically active agent to prevent or reduce intimal hyperplasia and a set of instructions explaining the use of the drug delivery vehicle.

ACTIVITY - Cytostatic; antithrombotic; antiinflammatory; ***antioxidant*** ; anticoagulant; immunosuppressive.

Young adult dogs (10 male, 2 female) were anaesthetized, heparinized and anticoagulated (at the surgeon's discretion) before the carotid artery was cross-clamped and an interpositional graft with end-to-side anastamoses of the femoral vein to the carotid artery was performed. Test and control articles were applied to a uniform thickness and allowed to harden. Grafts were placed in both carotid arteries by serial procedures. Balloon injury to the femoral arteries by three sequences of inflation and removal of a 4 French Fogarty catheter generated 5-cm lesions in each femoral artery that were or were not treated with test/control articles. The insertion site was repaired and the animal was closed. Post-operative care was performed by known methods along with prophylactic administration of antibiotics. For 7 days after surgery, animals received 250 mg/day aspirin. The wound site was debrided and temperature, heart rate and respiratory rates were monitored daily for 1 week following surgery. Angiography of the carotid sites was performed after surgery and monthly. Intravascular ultrasound (IVUS) was used to examine the vein grafts in 10 animals at the 12-week endpoint of the study. At the end of the experiments, the overall health was monitored, including routine blood work. Animals were anticoagulated and angiography and IVUS measurements of treated vessels were taken. Animals were anaesthetized and euthanized by known methods, the carotid arteries were exposed and the healing response was evaluated. The grafts, including anastamoses, were fixed under pressure in situ and were removed along with 4 cm of proximal and distal host vessel. Femoral arteries were exposed and the healing response observed. The femoral arteries were fixed under pressure and removed with distal and proximal host tissue. Femoral and carotid arteries were stored in 10 % neutral-buffered formalin until histology. The animals were assigned to test groups receiving:

(1) no treatment (control);
(2) fibrin vehicle;
(3) fibrin vehicle plus or minus micellar paclitaxel; and
(4) fibrin vehicle plus or minus microsphere paclitaxel.

In control animals, subcutaneous hematomas that resolved with time were observed in the carotid (1/3) and femoral (1/3) sites. Subcutaneous hematomas at the carotid site were also observed in animals treated with vehicle (2/3) and vehicle + paclitaxel (4/8)-these lesions resolved with time. A hematoma at the femoral site that reduced in size with time and healed well was present in 2/8 animals treated with paclitaxel. Two animals receiving the paclitaxel microcapsules were sacrificed before termination of the experiment because of uncontrolled bleeding at femoral and carotid sites, swellings at the left carotid area and altered mental status. Angiography showed that all carotid grafts were patent at the end of surgery and that the carotid grafts of surviving animals were patent at study end (12 weeks). Angiography at study end showed that both femoral arteries in 8/10 animals were patent; 2 appeared to be occluded at 12 weeks. IVUS showed patent vessels with some suggestion of intimal thickening in some samples. Paclitaxel limited stenosis at the proximal (P=0.08) and distal (P=0.09) anastomotic sites as assessed by angography at 12 weeks. For the carotid grafts, analysis of individual treatment groups showed that the fibrin vehicle alone also limited stenosis at the anastamotic sites, with healing in the vehicle and treated groups appearing to be similar. For the femoral grafts, angiography showed there was no significant difference between control, vehicle and paclitaxel treatment groups. Formulations containing paclitaxel had a 44 % larger lumen width (P at most 0.06) in the absence of changes in the intimal:medial ratio.

MECHANISM OF ACTION - Calcium channel blocker; converting enzyme inhibitor; cytokine inhibitor; growth factor inhibitor; growth factor sequestrant; fibrosis inhibitor; ***tissue*** ***factor*** ***inhibitor*** ; smooth muscle inhibitor; superoxide dismutase mimic; collagen synthesis inhibitor.

USE - The methods are used to prevent or reduce intimal hyperplasia, such as in vascular, intestinal and/or urinary systems (claimed) as well as organs such as the stomach, liver and intestines. They are used to prevent or reduce intimal hyperplasia at sites of insult, such as surgical insult including anastomoses following angioplasty, vascular reconstructive surgery, heart valve replacement and/or heart transplantation or in which a prosthesis (stent, graft and/or valve) is placed at the site of insult on the internal structure (claimed).

ADVANTAGE - The method is flexible enough to allow agents to be applied prior to or reapplied after surgery.
Dwg.0/0

TECH UPTX: 20011211
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The internal structure has a circular cross-section. The internal structure is a component of the vascular system, intestinal system and/or urinary system. The internal structure is a vascular structure and the surgical procedure is angioplasty, vascular reconstructive surgery, heart valve replacement and/or heart transplantation. The injury is a surgical injury, preferably that comprises placing a prosthesis, such as a stent, graft and/or valve, at the site of insult on the internal structure. The exterior surface of the vascular structure contacted with the drug delivery vehicle comprises both the prosthesis and the site of insult. The site of insult is an anastomosis. Preferred Compositions: The intimal hyperplasia preventing agent is an antithrombotic (heparin, heparin derivatives, hirudin and/or hirudin derivatives), antiinflammatory, corticosteroid (dexamethasone and/or its derivatives), antimicrotubule agent (taxane and/or its derivatives), antisense oligonucleotide, antineoplastic, ***antioxidant*** , antiplatelet agent or fibrosis inhibitor, (collagen synthesis inhibitor such as halofuginore or its derivatives and/or GpIIbIIIa), calcium channel blocker, converting enzyme inhibitor, cytokine inhibitor, growth factor, growth factor inhibitor, growth factor sequestering agent, immunosuppressive, ***tissue*** ***factor*** ***inhibitor*** , smooth muscle inhibitor, sulfated proteoglycan, superoxide dismutase mimic, nitric oxide and/or nitric oxide precursor. The drug delivery vehicle is a bioerodable, hydrogen, thermoreversible and/or bioresorbable vehicle, preferably a gel, foam, suspension, microcapsules, solid polymeric supports or fibrous structures. The bioresorbable component is insoluble in water, hydrophobic or hydrolytically and/or enzymatically cleavable. The bioresorbable component is a poly(ester), poly(hydroxy acid), poly(lactone), poly(amide), poly(ester-amide), poly(amino acid), poly(anhydride), poly(orthoester), poly(carbonate), poly(phosphazine), poly(phosphoester), poly(thioester) and/or polysaccharide, preferably a poly(hydroxy acid) such as poly(lactic acid), poly(glycolic acid), poly(caproic acid), poly(butyric acid), poly(valeric) acid, their copolymers and/or mixtures. The vehicle forms an excretable and/or metabolizable fragment. The gel is a thermoreversible gel, preferably comprising a Pluronic (RTM), fibrin sealant, albumin, collagen, gelatin, hydroxypropylmethylcellulose, organic polymer, polyethylene oxide, hyaluronic acid and/or polysaccharide. The gel comprises a polyurethane hydrogel or polyurethane-urea hydrogel. The drug delivery vehicle comprises fibrin, fibronectin and/or thrombin.

L7 ANSWER 24 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-536422 [59] WPIDS
DNN N2001-398432 DNC C2001-159678
TI Prosthetic heart valve comprises biologically active material in sewing ring, housing component, and/or valve component.
DC A96 B05 D22 P34
IN CUNANAN, C; HELMUS, M N; KAFESJIAN, R; TREMBLE, P
PA (EDWA-N) EDWARDS LIFESCIENCES CORP; (BAXT) BAXTER HEALTHCARE CORP
CYC 95
PI WO 2001054745 A2 20010802 (200159)* EN 38<--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001034583 A 20010807 (200174) <--
EP 1250165 A2 20021023 (200277) EN <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003520645 W 20030708 (200347) 52
US 2004093080 A1 20040513 (200432)
ADT WO 2001054745 A2 WO 2001-US2621 20010125; AU 2001034583 A AU 2001-34583 20010125; EP 1250165 A2 EP 2001-906708 20010125, WO 2001-US2621 20010125; JP 2003520645 W JP 2001-554728 20010125, WO 2001-US2621 20010125; US 2004093080 A1 Provisional US 2000-178084P 20000125, Div ex US 2000-571987 20000516, US 2003-700958 20031031
FDT AU 2001034583 A Based on WO 2001054745; EP 1250165 A2 Based on WO 2001054745; JP 2003520645 W Based on WO 2001054745
PRAI US 2000-571987 20000516; US 2000-178084P 20000125
AN 2001-536422 [59] WPIDS
AB WO 200154745 A UPAB: 20011012
NOVELTY - A prosthetic heart valve comprises sewing ring and a housing

component enclosing a valve component. The sewing ring, housing component, and/or valve component comprise biologically active material(s) to prevent tissue overgrowth.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for preventing or reducing tissue overgrowth of a prosthetic heart valve following implantation of the heart valve into a host comprises prior to implantation, incorporating into a component of the heart valve a biological active agent to prevent or retard tissue overgrowth; and

(2) a method for treating patients requiring heart valve replacement which comprises replacing an existing valve with a prosthetic valve comprising a biological active agent to prevent or retard tissue growth.

USE - As prosthetic heart valve. The invention is used for preventing or reducing tissue overgrowth of a prosthetic heart valve following implantation of the heart valve into a host comprises prior to implantation, incorporating into a component of the heart valve a biological active agent to prevent or retard tissue overgrowth; and for treating patients requiring heart valve replacement.

ADVANTAGE - The invention provides biologically active agents for preventing tissue overgrowth and has a decreased level of infiltration by recipient-derived fibrous fiber. The agents prevent excess fibrous tissue outgrowth on components of the valve, preferably without impeding tissue ingrowth which is desirably present to cover the exposed fabric of the sewing ring and to anchor the valve to the surrounding tissue. The invention improves quality and length of life of the patients.

Dwg.0/0

PI WO 2001054745 A2 20010802 (200159)* EN 38 A61L027-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001034583 A 20010807 (200174) A61L027-00 <--
EP 1250165 A2 20021023 (200277) EN A61L027-54 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003520645 W 20030708 (200347) 52 A61F002-24
US 2004093080 A1 20040513 (200432) A61F002-24

ADT WO 2001054745 A2 WO 2001-US2621 20010125; AU 2001034583 A AU 2001-34583 20010125; EP 1250165 A2 EP 2001-906708 20010125, WO 2001-US2621 20010125; JP 2003520645 W JP 2001-554728 20010125, WO 2001-US2621 20010125; US 2004093080 A1 Provisional US 2000-178084P 20000125, Div ex US 2000-571987 20000516, US 2003-700958 20031031

FDT AU 2001034583 A Based on WO 2001054745; EP 1250165 A2 Based on WO 2001054745; JP 2003520645 W Based on WO 2001054745

PRAI US 2000-571987 20000516; US 2000-178084P 20000125

TECH UPTX: 20011012

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The substrate is a polymer and reactive chemical functional groups are affixed to the surface of the substrate by plasma fixation.

TECHNOLOGY FOCUS - POLYMERS - Preferred Material: The sewing ring is made of a polymeric material from plastics and/or rubbers, or fabric comprising thermoplastic polyurethanes, nylons (preferably nylon-11 and/or nylon 12), polypropylene, polytetrafluoroethylene, polyesters (preferably polyethylene terephthalate), nylon polymers, block copolymers of a polyether polymer and a polyester polymer, and block copolymers of a polyether polyol, or polyamides, polyimides, polyolefins (preferably polyethylenes or polypropylenes), synthetic hydrocarbon elastomers, or natural rubber.

The biologically active material is layered with a coating from bioerodable, hydrogel, thermoreversible, and/or bioresorbable coatings. The coatings are also made of gels, foams, suspensions, microcapsules, solid polymeric supports, or fibrous structures.

The bioresorbable component is poly(esters), poly(hydroxy) acids, poly(lactones), poly(amides), poly(ester-amides), poly(amino acids), poly(anhydrides), poly(orthoesters), poly(carbonates), poly(phosphazines), poly(phosphoesters), poly(alkylene oxides) poly(thioesters), polysaccharides, and/or proteins. The poly(hydroxy) acid is made of poly(lactic) acid, poly(glycolic) acid, poly(caproic) acid, poly(butyric) acid, poly(valeric) acid and/or copolymers.

The gel is a thermoreversible gel from pluronics, fibrin sealants, albumin, collagen, gelatin, hydroxypropylmethylcellulose, polyethylene oxide, hyalouronic acid, and/or polysaccharides. It also comprises polyurethane hydrogels, or polyurethane-urea hydrogels.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Component: The biologically active material is antithrombotics, antiinflammatories, corticosteroids, antimicrotubule agents, antisense oligonucleotides, antineoplastics, ***antioxidants*** , antiplatelets, calcium channel blockers, converting enzyme inhibitors, cytokine inhibitors, growth factors, growth factor inhibitors, growth factor sequestering agents, immunosuppressives, ***tissue*** ***factor*** ***inhibitor*** , smooth muscle inhibitors, organoselenium compounds, retinoic acid, retinoid compounds, sulfated proteoglycans, nitrogen oxide (NO) and/or NO precursors.
The antithrombotic is heparin, hirudin, and/or their derivatives.
The corticosteroid is dexamethasone and/or its derivatives.
The antimicrotubule agent is taxane and/or its derivatives.
The antiplatelet agent is an inhibitor of collagen synthesis.
The inhibitor of collagen synthesis is halofuginore and/or its derivatives.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Component: The biologically active material is combined with a surfactant from benzalkonium halides or sterylalkonium halides. It also comprises taxane or its derivatives. It is bonded to a reactive group from amine-containing, hydroxyl, carboxyl, and/or carbonyl. The amine-containing groups are amino, amido, urethane, and/or urea.
The amino groups are primary or secondary amino. They are derived from a nitrogen-containing gas from ammonia, organic amines, nitrous oxide, and/or nitrogen.
The organic amines are methylamine, dimethylamine, ethylamine, diethylamine, n-propylamine, allylamine, isopropylamine, n-butylamine, n-butylmethylamine, n-amylamine, 2-ethylhexylamine, ethylenediamine, 1,4-butanediamine, 1,6-hexanediamine, cyclohexylamine, N-methylcyclohexylamine, or ethyleneimine. The biologically active material is encapsulated by a microcapsule from sodium alginate envelope.

TECHNOLOGY FOCUS - TEXTILES AND PAPER - Preferred Structure: The fabric is weft knit, warp knit, and/or weave structure, each with/without a velour.

L7 ANSWER 25 OF 27 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN
AN 2001-0366468 PASCAL

TIEN Hepatic response to sepsis : Interaction between coagulation and inflammatory processes
Sepsis: interface between inflammation, coagulation, and the endothelium
AU DHAINAUT Jean-Francois; MARIN Nathalie; MIGNON Alexandre; VINSONNEAU Christophe
CS Medical Intensive Care Unit, Cochin Port-Royal University-Hospital, AP-HP, Paris V University, Paris, France
Eli Lilly and Company, Indianapolis, IN, United States (patr.)
SO Critical care medicine, ***(2001)*** , 29(7, SUP), S42-S47, 63 refs.
Conference: 2 The Margaux Conference on Critical Illness, Margaux (France), 8 Nov 2000
ISSN: 0090-3493 CODEN: CCMDC7
DT Journal; Conference
BL Analytic
CY United States
LA English
AV INIST-17751, 354000099037910090

AB Objectives: a) To review the hepatic response to sepsis and to establish how this response contributes to coagulation and inflammatory processes; b) to review the physiologic and biochemical mechanisms that suggest hepatic dysfunction may occur during sepsis, enhance procoagulant and proinflammatory activities, and participate in the potential evolution to multiple organ dysfunction syndrome. Data Sources: A summary of published medical literature from MEDLINE search files and published reviews on liver function in experimental and human sepsis. Data Summary: In sepsis, the liver plays a major role in host defense mechanisms. Kupffer cells are responsible for bacterial ***scavenging*** , bacterial products inactivation, and inflammatory mediators clearance and production. Hepatocytes, via receptors for many proinflammatory cytokines, modify their metabolic pathway toward gluconeogenesis, amino-acid uptake, and increased synthesis of coagulant and complement factors and protease inhibitors. The acute-phase protein (APP) response also contributes to the procoagulant state, especially by enhancing the inhibition of protein C (.alpha..sub.1-antitrypsin and .alpha..sub.2-macroglobulin) and by decreasing liver synthesis of protein C and antithrombin (negative APPs). Elevated C-reactive protein levels (positive APPs) promote the expression of tissue factor by mononuclear cells. Increased liver production of

thrombin-activatable fibrinolytic inhibitor (positive APPs) enhances fibrinolysis inhibition. Conversely, such hepatic inflammatory and coagulation processes in sepsis may alter the function of this organ. Indeed, the liver can be injured by activated Kupffer cells that release chemokines, attract blood neutrophils into the liver, and activate them. Neutrophils up-regulate their surface adhesion molecules, tissue factor, and Kupffer cells, whereas ***tissue*** ***factor*** ***pathway*** ***inhibitor*** and thrombomodulin are almost undetectable in endothelial cells. This may lead to microcirculatory disturbances, fibrin deposition, hepatocyte injury, endotoxin and bacteria spillover, and multiple organ failure. Conclusions: In sepsis, the liver participates in host defense and tissue repair through hepatic cell cross-talk that controls most of the coagulation and inflammatory processes. When this control is not adequate, a secondary hepatic dysfunction may occur and may sometimes lead to bacterial products spillover, enhanced procoagulant and inflammatory processes, and in turn, multiple organ failure and death.

SO Critical care medicine, ***(2001)*** , 29(7, SUP), S42-S47, 63 refs. Conference: 2 The Margaux Conference on Critical Illness, Margaux (France), 8 Nov 2000
ISSN: 0090-3493 CODEN: CCMDC7

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L7 ANSWER 26 OF 27 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN

AN 2002:30618 DISSABS Order Number: AAI3033405

TI Characterization and effects of metal- ***chelate*** -heparin complexes with relevance to vascular restenosis

AU Aceituno Alvarez, Alexis Roobins [Ph.D.]; Dadey, Eric [adviser]
CS University of Illinois at Chicago, Health Sciences Center (0806)

SO Dissertation Abstracts International, (***2001***) Vol. 62, No. 11B, p. 5055. Order No.: AAI3033405. 130 pages.
ISBN: 0-493-45632-5.
DT Dissertation
FS DAI
LA English

AB The interaction between metal ***chelate*** compounds and heparin was investigated using spectroscopic and chemical techniques, and the effect of metal ***chelate*** binding on ex vivo and in vivo effects of heparin determined in a rat model of restenosis. It was found that iron (III) acetylacetone interacts preferentially with heparin in a 1:1 mole

ratio of iron ***chelate*** /hexosamine residue. Binding was the result of a combination of electrostatic and non-electrostatic forces. The association of iron acetylacetone and heparin was confirmed by light scattering showing the formation of a complex of high molecular weight.

Ex vivo studies indicated no difference in activity against thrombin and factor Xa between the complex and heparin alone; however, a protective role of complexed heparin against the effect of metal ions on LDL oxidation was observed.

In vivo studies revealed that the formation of the iron acetylacetone-heparin complex changed the kinetics of disposition of heparin after intravenous administration to rats apparently as a result of increased binding to endothelium. In addition, the antiproliferative effects of the complex were assessed in a rat carotid artery model of restenosis induced by air. Histological analysis of carotid artery segments showed that air effectively damaged the endothelial lining and the rate of endothelial regeneration was faster in drug treated groups compared to control. Finally, the rate of smooth muscle cell proliferation, measured by the extent of arterial wall thickening, was evaluated by monitoring a marker of thrombosis (***Tissue*** ***Factor*** ***Pathway*** ***inhibitor*** , TFPI) and a marker of vascular damage (fibronectin, FN). Metal- ***chelate*** heparin complex produced a sustained depletion of plasma TFPI activity compared to heparin alone in a seven-day experimental period. This result was explained as heparin changes in its kinetics of disposition. A correlation between the extent of vascular proliferation and FN levels was evidenced in no drug treated group indicating that FN may have the potential of a circulating marker of restenosis progression. Results from heparin treated and complex treated groups showed no significant differences and steady levels of FN. These results were corroborated by histological cross section analysis of treated segments.

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L7 ANSWER 27 OF 27 JICST-EPlus COPYRIGHT 2004 JST on STN
AN 1010998554 JICST-EPlus
TI ***Tissue*** ***Factor*** ***Pathway*** ***Inhibitor*** as a Universal Anticoagulant for Use in Clinical Laboratory Tests.
AU TSUJI R; TATSUMI N; HINO M; NISHIOKA T; TAKUBO T
CS Osaka City Univ., Osaka

SO Tohoku J Exp Med, (2001) vol. 194, no. 3, pp. 165-174. Journal Code: G0649A (Fig. 3, Tbl. 3, Ref. 24)
CODEN: TJEMAO; ISSN: 0040-8727
CY Japan
DT Journal; Article
LA English
STA New
AB ***Tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI) is a protease inhibitor of extrinsic coagulation. The present study investigates the possibility of utilizing TFPI as a universal anticoagulant in clinical laboratory tests. The optimal concentration of TFPI for use in clinical laboratory tests was found to be 1 .MU.l TFPI/ml blood (100 mmol TFPI/ml blood); the subsequent analyses were conducted at this concentration. In hematological tests, complete blood cell count and differential white blood cell count were done with an automatic blood analyzer. The results except for platelet and white blood cell counts were similar for ethylenediaminetetraacetic acid (EDTA)-treated and TFPI-treated samples. The effects of TFPI on platelet count were more pronounced when blood samples were stored at 4.DEG.C. than at room temperature. The effects of TFPI on cell morphology were evaluated by spreading blood samples into thin films and applying a Giemsa stain. The results showed that TFPI did not alter the morphology of blood cells. An automatic biochemical analyzer performed seventeen basic biochemical tests on serum samples and TFPI-treated plasma samples. The results of seventeen tests were comparable between TFPI-treated samples and EDTA-treated samples. The prothrombin time for TFPI-treated plasma samples was longer than that for citrated plasma samples. Nonetheless, in activated partial thromboplastin time tests, the addition of the reagent caused turbidity and partial coagulation, thus demonstrating that TFPI is not suitable for this assay. These findings suggest that although some tests cannot be performed with TFPI, this compound may be useful as a universal anticoagulant in the future. (author abst.)
TI ***Tissue*** ***Factor*** ***Pathway*** ***Inhibitor*** as a Universal Anticoagulant for Use in Clinical Laboratory Tests.
SO Tohoku J Exp Med, (2001) vol. 194, no. 3, pp. 165-174. Journal Code: G0649A (Fig. 3, Tbl. 3, Ref. 24)
CODEN: TJEMAO; ISSN: 0040-8727
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CT anticoagulant; thromboplastin; proteinase inhibitor; reagent for clinical test; hematologic test; ***chelating*** reagent; aminocarboxylic acid; diamine; aliphatic amine; aliphatic carboxylic acid

=> file hcaplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	123.01	153.78

FILE 'HCAPLUS' ENTERED AT 11:04:12 ON 02 SEP 2004

FILE COVERS 1907 - 2 Sep 2004 VOL 141 ISS 10
FILE LAST UPDATED: 1 Sep 2004 (20040901/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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=> s l5
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          1169 "BLOODS"/BI
       1149299 "BLOOD"/BI
                 (("BLOOD" OR "BLOODS")/BI)
         96803 "COAGULATION"/BI
           187 "COAGULATIONS"/BI
         96863 "COAGULATION"/BI
                 (("COAGULATION" OR "COAGULATIONS")/BI)
        752764 "FACTORS"/BI
         10321 "EPI"/BI
            28 "EPIS"/BI
         10338 "EPI"/BI
                 (("EPI" OR "EPIS")/BI)
         13707 "EXTRINSIC"/BI
             1 "EXTRINSICS"/BI
         13707 "EXTRINSIC"/BI
                 (("EXTRINSIC" OR "EXTRINSICS")/BI)
        216120 "PATHWAY"/BI
        145615 "PATHWAYS"/BI
        323969 "PATHWAY"/BI
                 (("PATHWAY" OR "PATHWAYS")/BI)
        450629 "INHIBITOR"/BI
        469611 "INHIBITORS"/BI
        724704 "INHIBITOR"/BI
                 (("INHIBITOR" OR "INHIBITORS")/BI)
            10 "BLOOD-COAGULATION FACTORS, EPI (EXTRINSIC PATHWAY INHIBITOR)"/B
               I
                 (("BLOOD"(W)"COAGULATION"(W)"FACTORS"(W)"EPI"(W)"EXTRINSIC"(W)
                 "PATHWAY"(W)"INHIBITOR")/BI)
       1149184 "BLOOD"/BI
          1169 "BLOODS"/BI
       1149299 "BLOOD"/BI
                 (("BLOOD" OR "BLOODS")/BI)
         96803 "COAGULATION"/BI
           187 "COAGULATIONS"/BI
         96863 "COAGULATION"/BI
                 (("COAGULATION" OR "COAGULATIONS")/BI)
        752764 "FACTORS"/BI
          1335 "LACI"/BI
            23 "LACIS"/BI
          1354 "LACI"/BI
                 (("LACI" OR "LACIS")/BI)
           231 "BLOOD-COAGULATION FACTORS, LACI"/BI
                 (("BLOOD"(W)"COAGULATION"(W)"FACTORS"(W)"LACI")/BI)
       1149184 "BLOOD"/BI
          1169 "BLOODS"/BI
       1149299 "BLOOD"/BI
                 (("BLOOD" OR "BLOODS")/BI)
         96803 "COAGULATION"/BI
           187 "COAGULATIONS"/BI
         96863 "COAGULATION"/BI
                 (("COAGULATION" OR "COAGULATIONS")/BI)
        752764 "FACTORS"/BI
         66130 "LIPOPROTEIN"/BI
         72874 "LIPOPROTEINS"/BI
         90462 "LIPOPROTEIN"/BI
                 (("LIPOPROTEIN" OR "LIPOPROTEINS")/BI)
        842901 "ASSOCD"/BI
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        2 "ASSOCDS"/BI
   842902 "ASSOCD"/BI
            (("ASSOCD" OR "ASSOCDS")/BI)
    96803 "COAGULATION"/BI
      187 "COAGULATIONS"/BI
    96863 "COAGULATION"/BI
            (("COAGULATION" OR "COAGULATIONS")/BI)
   469611 "INHIBITORS"/BI
        1 "BLOOD-COAGULATION FACTORS, LIPOPROTEIN-ASSOCD. COAGULATION
          INHIBITORS"/BI
            (("BLOOD"(W)"COAGULATION"(W)"FACTORS"(W)"LIPOPROTEIN"(W)"ASSOC
            D"(W)"COAGULATION"(W)"INHIBITORS")/BI)
  1149184 "BLOOD"/BI
     1169 "BLOODS"/BI
  1149299 "BLOOD"/BI
            (("BLOOD" OR "BLOODS")/BI)
    96803 "COAGULATION"/BI
      187 "COAGULATIONS"/BI
    96863 "COAGULATION"/BI
            (("COAGULATION" OR "COAGULATIONS")/BI)
   752764 "FACTORS"/BI
      200 "TFI"/BI
        4 "TFIS"/BI
      203 "TFI"/BI
            (("TFI" OR "TFIS")/BI)
        0 "BLOOD-COAGULATION FACTORS, TFI"/BI
            (("BLOOD"(W)"COAGULATION"(W)"FACTORS"(W)"TFI")/BI)
    10321 "EPI"/BI
       28 "EPIS"/BI
    10338 "EPI"/BI
            (("EPI" OR "EPIS")/BI)
  1149184 "BLOOD"/BI
     1169 "BLOODS"/BI
  1149299 "BLOOD"/BI
            (("BLOOD" OR "BLOODS")/BI)
    96803 "COAGULATION"/BI
      187 "COAGULATIONS"/BI
    96863 "COAGULATION"/BI
            (("COAGULATION" OR "COAGULATIONS")/BI)
   752764 "FACTORS"/BI
        0 "EPI BLOOD-COAGULATION FACTORS"/BI
            (("EPI"(W)"BLOOD"(W)"COAGULATION"(W)"FACTORS")/BI)
    13707 "EXTRINSIC"/BI
        1 "EXTRINSICS"/BI
    13707 "EXTRINSIC"/BI
            (("EXTRINSIC" OR "EXTRINSICS")/BI)
   216120 "PATHWAY"/BI
   145615 "PATHWAYS"/BI
   323969 "PATHWAY"/BI
            (("PATHWAY" OR "PATHWAYS")/BI)
   450629 "INHIBITOR"/BI
   469611 "INHIBITORS"/BI
   724704 "INHIBITOR"/BI
            (("INHIBITOR" OR "INHIBITORS")/BI)
  1149184 "BLOOD"/BI
     1169 "BLOODS"/BI
  1149299 "BLOOD"/BI
            (("BLOOD" OR "BLOODS")/BI)
    96803 "COAGULATION"/BI
      187 "COAGULATIONS"/BI
    96863 "COAGULATION"/BI
            (("COAGULATION" OR "COAGULATIONS")/BI)
   752764 "FACTORS"/BI
        0 "EXTRINSIC PATHWAY INHIBITOR BLOOD-COAGULATION FACTORS"/BI
            (("EXTRINSIC"(W)"PATHWAY"(W)"INHIBITOR"(W)"BLOOD"(W)"COAGULATI
            ON"(W)"FACTORS")/BI)
     1335 "LACI"/BI
       23 "LACIS"/BI
     1354 "LACI"/BI
            (("LACI" OR "LACIS")/BI)
  1149184 "BLOOD"/BI
     1169 "BLOODS"/BI
  1149299 "BLOOD"/BI
            (("BLOOD" OR "BLOODS")/BI)
    96803 "COAGULATION"/BI
      187 "COAGULATIONS"/BI
    96863 "COAGULATION"/BI
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          (("COAGULATION" OR "COAGULATIONS")/BI)
  752764 "FACTORS"/BI
       0 "LACI BLOOD-COAGULATION FACTORS"/BI
          (("LACI"(W)"BLOOD"(W)"COAGULATION"(W)"FACTORS")/BI)
   66130 "LIPOPROTEIN"/BI
   72874 "LIPOPROTEINS"/BI
   90462 "LIPOPROTEIN"/BI
          (("LIPOPROTEIN" OR "LIPOPROTEINS")/BI)
  842901 "ASSOCD"/BI
       2 "ASSOCDS"/BI
  842902 "ASSOCD"/BI
          (("ASSOCD" OR "ASSOCDS")/BI)
   96803 "COAGULATION"/BI
     187 "COAGULATIONS"/BI
   96863 "COAGULATION"/BI
          (("COAGULATION" OR "COAGULATIONS")/BI)
  450629 "INHIBITOR"/BI
  469611 "INHIBITORS"/BI
  724704 "INHIBITOR"/BI
          (("INHIBITOR" OR "INHIBITORS")/BI)
     260 "LIPOPROTEIN-ASSOCD. COAGULATION INHIBITOR"/BI
          (("LIPOPROTEIN"(W)"ASSOCD"(W)"COAGULATION"(W)"INHIBITOR")/BI)
   66130 "LIPOPROTEIN"/BI
   72874 "LIPOPROTEINS"/BI
   90462 "LIPOPROTEIN"/BI
          (("LIPOPROTEIN" OR "LIPOPROTEINS")/BI)
  842901 "ASSOCD"/BI
       2 "ASSOCDS"/BI
  842902 "ASSOCD"/BI
          (("ASSOCD" OR "ASSOCDS")/BI)
   968[illegible] "COAGULATION"/BI
     18[illegible] "COAGULATIONS"/BI
   968[illegible] "COAGULATION"/BI
          (("COAGULATION" OR "COAGULATIONS")/BI)
  46961[illegible] "INHIBITORS"/BI
 114918[illegible] "BLOOD"/BI
    116[illegible] "BLOODS"/BI
 11492[illegible] "BLOOD"/BI
          (("BLOOD" OR "BLOODS")/BI)
   968[illegible] "COAGULATION"/BI
     18[illegible] "COAGULATIONS"/BI
   968[illegible] "COAGULATION"/BI
          (("COAGULATION" OR "COAGULATIONS")/BI)
   7527[illegible] "FACTORS"/BI
        [illegible] "LIPOPROTEIN-ASSOCD. COAGULATION INHIBITORS BLOOD-COAGULATION
          FACTORS"/BI
          (("LIPOPROTEIN"(W)"ASSOCD"(W)"COAGULATION"(W)"INHIBITORS"(W)"B
          LOOD"(W)"COAGULATION"(W)"FACTORS")/BI)
  610733 "TISSUE"/BI
  301240 "TISSUES"/BI
  780021 "TISSUE"/BI
          (("TISSUE" OR "TISSUES")/BI)
  850220 "FACTOR"/BI
  752764 "FACTORS"/BI
 1343616 "FACTOR"/BI
          (("FACTOR" OR "FACTORS")/BI)
  450629 "INHIBITOR"/BI
  469611 "INHIBITORS"/BI
  724704 "INHIBITOR"/BI
          (("INHIBITOR" OR "INHIBITORS")/BI)
     143 "TISSUE FACTOR INHIBITOR"/BI
          (("TISSUE"(W)"FACTOR"(W)"INHIBITOR")/BI)
  610733 "TISSUE"/BI
  301240 "TISSUES"/BI
  780021 "TISSUE"/BI
          (("TISSUE" OR "TISSUES")/BI)
  850220 "FACTOR"/BI
  752764 "FACTORS"/BI
 1343616 "FACTOR"/BI
          (("FACTOR" OR "FACTORS")/BI)
  216120 "PATHWAY"/BI
  145615 "PATHWAYS"/BI
  323969 "PATHWAY"/BI
          (("PATHWAY" OR "PATHWAYS")/BI)
  450629 "INHIBITOR"/BI
  469611 "INHIBITORS"/BI
  724704 "INHIBITOR"/BI
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              (("INHIBITOR" OR "INHIBITORS")/BI)
        1000 "TISSUE FACTOR PATHWAY INHIBITOR"/BI
              (("TISSUE"(W)"FACTOR"(W)"PATHWAY"(W)"INHIBITOR")/BI)
         603 194554-71-7
      121134 CHELAT?
       46245 SCAVENG?
      646974 OXYGEN
        6326 OXYGENS
      651388 OXYGEN
              (OXYGEN OR OXYGENS)
       94260 DISPLACEMENT
       17803 DISPLACEMENTS
      107298 DISPLACEMENT
              (DISPLACEMENT OR DISPLACEMENTS)
     1375366 GAS
      473558 GASES
     1545218 GAS
              (GAS OR GASES)
           0 OXYGEN DISPLACEMENT GAS
              (OXYGEN(W)DISPLACEMENT(W)GAS)
      120870 ANTIOX?
L8        20 L2 AND L3

=> d bib abs 1-20

L8   ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:610099  HCAPLUS
DN   141:162356
TI   Stabilized aqueous compositions comprising   ***tissue***     ***factor***
       ***pathway***     ***inhibitor***   (TFPI) or   ***tissue***
       ***factor***     ***pathway***     ***inhibitor***   variant
IN   Chen, Bao-lu
PA   Chiron Corporation, USA
SO   PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
PI   WO 2004062689         A1    20040729    WO 2004-US233            20040108
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB,
             BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR,
             CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG,
             ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU,
             ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ,
             KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN,
             MW, MX, MX, MZ
PRAI US 2003-438519P      P     20030108
     US 2003-494577P      P     20030813
     US 2003-509260P      P     20031008
     US 2003-512090P      P     20031020
AB   Stabilized aq. compns. of   ***tissue***     ***factor***
       ***pathway***     ***inhibitor***   (TFPI) or TFPI variants comprise a
     solubilizing agent, an   ***antioxidant***   , and a buffer.  The
     combination of a solubilizing agent and an   ***antioxidant***   can lead
     to a significant improvement in the storage life of TFPI or TFPI variant
     compns.  The solubilizing agent and   ***antioxidant***   substantially
     counteract the effects of TFPI or TFPI variant degrdn. through aggregation
     and oxidn.

L8   ANSWER 2 OF 20  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:510134  HCAPLUS
DN   141:52871
TI   Pharmaceutical composition of interferon gamma with molecular diagnostics
     for the improved treatment of bronchial asthma
IN   Bevec, Dorian; Ziesche, Rolf
PA   Mondobiotech Laboratories Anstalt, Liechtenstein
SO   Eur. Pat. Appl., 23 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
PI   EP 1430902           A1     20040623    EP 2002-28574            20021220
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
```

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRAI EP 2002-28574 20021220
AB The disclosed invention relates to a novel pharmaceutical compn. comprising interferon-.gamma. and a diagnostic array of candidate polynucleotides for the improved treatment of lung diseases, esp. for all forms of bronchial asthma. This invention describes the combination of mol. diagnosis and clin. therapy as a novel medication principle for redn. of mortality and improvement of disease management in bronchial asthma.

L8 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:355085 HCAPLUS
DN 140:369944
TI Human tissue-specific housekeeping genes identified by expression profiling
IN Aburatani, Hiroyuki; Yamamoto, Shogo
PA NGK Insulators, Ltd., Japan
SO PCT Int. Appl., 372 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004035785	A1	20040429	WO 2002-JP10753	20021016

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2002-JP10753 20021016
AB Housekeeping genes commonly expressed in 35 different human tissues, oligonucleotide probes and DNA microarrays contg. them, are disclosed.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:266918 HCAPLUS
DN 140:282485
TI Methods for diagnosing interstitial lung diseases using biomarkers identified by microarray gene expression profiling
IN Bevec, Dorian
PA Mondobiotech SA, Switz.
SO Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1403638	A1	20040331	EP 2002-21413	20020925

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRAI EP 2002-21413 20020925
AB The present invention relates to mol. methods diagnosing interstitial lung diseases (ILDs) using microarrays of candidate polynucleotides. The present invention also relates to methods useful in mol. evaluation of the efficacy of a drug applied to a person in need suffering from an ILD by gene expression profiling images. An aspect of the invention relates to the use of polynucleotide arrays, which allows to quant. study mRNA expression levels of selected candidate genes in human biopsies. A method for detecting gene expression of infective agents from patients with ILD is also disclosed.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:991351 HCAPLUS
DN 140:23246
TI Combination treatments for purinoceptor-related disorders
IN Wilson, Constance N.; Sirgo, Mark A.
PA Endacea, Inc., USA
SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003103675	A2	20031218	WO 2003-US17964	20030606
WO 2003103675	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-386769P P 20020606
OS MARPAT 140:23246
AB The present invention provides methods of preventing and treating purinoceptor-related disorders comprising concurrently administering an A1 adenosine receptor antagonist or a P2x purinoceptor antagonist with an at least one addnl. active agent effective to treat purinoceptor-related disorders. The present invention also provides pharmaceutical formulations suitable for preventing and treating purinoceptor-related disorders. Blocking activation of purinergic receptors may be effective for the prevention and early treatment of allergic asthma (both bronchoconstriction and innflammation) without the side effects assocd. with many current therapies.

L8 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:875393 HCAPLUS
DN 139:363045
TI Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics
IN Nevins, Joseph; West, Mike; Goldschmidt, Pascal
PA Duke University, USA
SO PCT Int. Appl., 408 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003091391	A2	20031106	WO 2002-US38221	20021112

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003091391	A2	20031106	WO 2002-XA38221	20021112

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003091391	A2	20031106	WO 2002-XB38221	20021112

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2003224383	A1	20031204	US 2002-291885	20021112
PRAI	US 2002-374547P	P	20020423		
	US 2002-420784P	P	20021024		
	US 2002-421043P	P	20021025		
	US 2002-424680P	P	20021108		
	WO 2002-US38221	A	20021112		

AB Genes whose expression is correlated with an determinant of an atherosclerotic phenotype are provided. Also provided are methods of using the subject atherosclerotic determinant genes in diagnosis and treatment methods, as well as drug screening methods. In addn., reagents and kits thereof that find use in practicing the subject methods are provided. Also provided are methods of detg. whether a gene is correlated with a disease phenotype, where correlation is detd. using a Bayesian anal.

L8 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:491063 HCAPLUS
DN 139:57897
TI Novel pharmaceutical composition of interferon gamma or pirfenidone combined with molecular diagnostics for the improved treatment of interstitial lung diseases
IN Bey[illegible], Dorian; Ziesche, Rolf
PA Mondobiotech SA, Switz.
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051388	A2	20030626	WO 2002-CH691	20021212
WO 2003051388	A3	20031030		

DS AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	NO 2003003642	A	20031017	NO 2003-3642	20030815
	PRAI US 2001-130011	A	20011218		
	WO 2002-CH691	W	20021212		

AB The present invention relates to a novel pharmaceutical compn. of compds. having the biol. activity of interferon gamma (IFN-.gamma.) or pirfenidone in combination with a diagnostic array of candidate polynucleotides for the improved treatment of all forms of interstitial lung diseases, in particular of idiopathic pulmonary fibrosis (IPF). This invention describes the combination of mol. diagnosis and clin. therapy as a novel medication principle for redn. of mortality and improvement of disease management in interstitial lung diseases.

L8 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:462625 HCAPLUS
DN 139:212285
TI Relationship between oxidative stress and extrinsic coagulation pathway in haemodialyzed patients
AU Pawlak, Krystyna; Borawski, Jacek; Naumnik, Beata; Mysliwiec, Michal
CS Department of Nephrology and Internal Medicine, Medical University of Bialystok, Bialystok, 15-540, Pol.
SO Thrombosis Research (2003), 109(5-6), 247-251
CODEN: THBRAA; ISSN: 0049-3848
PB Elsevier Science Inc.
DT Journal
LA English
AB Enhanced oxidative stress (SOX), endothelial dysfunction and hemostatic abnormalities are common in end-stage renal failure patients undergoing maintenance hemodialysis (HD). We studied assocns. among circulating immunoreactive total lipid peroxides as a marker of short-time SOX, autoantibodies against oxidized LDL as a surrogate of prolonged SOX, copper/zinc superoxide dismutase (Cu/Zn SOD) as a major ***antioxidant*** enzyme, tissue factor (TF) as a principal initiator of extrinsic coagulation pathway counteracted by its inhibitor (TFPI), and

prothrombin fragment 1+2 (F 1+2) as a surrogate of activated hemostasis. Pre-dialysis blood levels of all the markers studied were higher in 24 clin. stable HD patients compared to 11 healthy controls. Spearman's correlations among the 3 SOX markers were pos. but nonsignificant in both HD patients and controls. In HD subjects, increased Cu/Zn SOD levels directly correlated with those of TF (rho=0.551, p=0.005) and TFPI (rho=0.501, p=0.001); the coagulation markers were also pos. assocd. with each other (rho=0.663, p=0.0004). In healthy subjects, the relations between Cu/Zn SOD, TF and TFPI levels were inverse but not significant, and the direct assocn. between TF and TFPI was nonsignificant either. In conclusion, increased plasma levels of Cu/Zn SOD, the ***antioxidant*** enzyme with emerging endothelial cell-protective and antithrombotic properties, may be a novel part of the system counteracting activated extrinsic coagulation system in maintenance HD patients.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:230774 HCAPLUS
DN 139:95136
TI Vascular thrombogenicity induced by progressive LDL oxidation: Protection by ***antioxidants***
AU Banfi, Cristina; Camera, Marina; Giandomenico, Giovanna; Toschi, Vincenzo; Arpaia, Magda; Mussoni, Luciana; Tremoli, Elena; Colli, Susanna
CS Department of Pharmacological Sciences, E. Grossi Paoletti Center, University of Milan, Milan, Italy
SO Thrombosis and Haemostasis (2003), 89(3), 544-553
CODEN: THHADQ; ISSN: 0340-6245
PB Schattauer GmbH
DT Journal
LA English
AB Oxidative modification of LDL, which dysregulates the homeostasis between blood and vascular cells, and alterations of endothelial function are considered among the early events in the pathogenesis of atherosclerosis. This study was designed to evaluate the impact of progressive LDL oxidn. on the thrombotic response both in vitro and in vivo, and to address the potential effect of ***antioxidants*** . Tissue factor was induced by progressive LDL oxidn. in HUVEC, and this event was in parallel to the appearance of the apoptotic phenotype. Both these phenomena were mediated by ERK1/2 activation and were prevented by LDL pre-enrichment with ***antioxidants*** . In contrast, ***antioxidants*** failed to affect tPA and PAI-1 secretion, which was increased by LDL, either native or oxidized. ***Tissue*** ***factor*** - ***pathway*** ***inhibitor*** was also increased upon HUVEC exposure to progressively oxidized LDL; LDL, in the presence of an oxidative agent, trigger a thrombogenic response in vivo, mostly TF-dependent, in an in situ model of platelet deposition. This effect was markedly attenuated when LDL were enriched with ***antioxidants*** . It can be concluded that vascular thrombogenicity is induced by progressive LDL oxidn. and that alterations of the ***antioxidant*** /oxidant balance of the LDL particle in favor of the ***antioxidant*** tone are protective against the thrombotic response triggered by oxidative stress. The extrapolation of these data in a clin. setting, even if not easy, offers potential insights for the use of ***antioxidants*** in the prevention of thrombotic complications assocd. with atherothrombosis.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:778080 HCAPLUS
DN 137:275375
TI Rapid assessment of coagulation activity in whole blood
IN Post, Diane; Benecky, Michael; Moskowitz, Keith
PA Coagulation Diagnostics, Incorporated, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002079375	A1	20021010	WO 2002-US9584	20020329
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2003064414	A1	20030403	US 2002-107409	20020328
PRAI	US 2001-279737P	P	20010330		

AB The present invention is directed to methods to rapidly assess the overall coagulant properties of a patient's blood sample by inhibiting the activation of the intrinsic contact activation pathway of coagulation and activating the extrinsic pathway of coagulation. When the sample is whole blood, the resulting clotting time represents the overall coagulant activity of the plasma and cellular components of the blood, which is indicative of existing or impending pathol. arising from abnormal coagulability. The invention also provides a method for measuring the risk of a patient for a thrombotic event and for monitoring the effectiveness of procoagulant/anticoagulant therapy.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:574958 HCAPLUS
DN 137:135087
TI Combinations of sterol absorption inhibitor(s) with blood modifier(s) for treating vascular conditions
IN Kosoglou, Teddy; Ress, Rudyard Joseph; Strony, John; Veltri, Enrico P.
PA Schering Corporation, USA
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002058734	A2	20020801	WO 2002-US2013	20020125
	WO 2002058734	A3	20030703		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002147184	A1	20021010	US 2002-56680	20020125
	EP 1353694	A2	20031022	EP 2002-704233	20020125
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2002006639	A	20040225	BR 2002-6639	20020125
	EP 1413331	A2	20040428	EP 2004-161	20020125
	EP 1413331	A3	20040630		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004517920	T2	20040617	JP 2002-559068	20020125
	US 2002192203	A1	20021219	US 2002-136968	20020501
	NO 2003003357	A	20030925	NO 2003-3357	20030725
	US 2004097482	A1	20040520	US 2003-639900	20030813
PRAI	US 2001-264275P	P	20010126		
	US 2001-264396P	P	20010126		
	US 2001-264600P	P	20010126		
	US 2001-324123P	P	20010921		
	US 2001-323839P	P	20010921		
	US 2001-323842P	P	20010921		
	EP 2002-714773	A3	20020125		
	US 2002-57323	A3	20020125		
	US 2002-57646	A1	20020125		
	WO 2002-US2013	W	20020125		

OS MARPAT 137:135087

AB The present invention provides compns., therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor administered in an amt. of 0.1-1000 mg/day; and (b) at least one blood modifier administered in an amt. of 1-1000 mg/day, which can be useful for treating vascular conditions, e.g., diabetes and obesity, and lowering plasma levels of sterols in mammals. A sterol absorption inhibitor is an azetidinone compd. or a .beta.-lactam, while a blood modifier was selected from anticoagulants, antithrombotics, fibrinogen receptor antagonists, platelet aggregation inhibitors, hemorheol. agents, ***lipoprotein***

assocd . ***coagulation*** ***inhibitors*** , Factor VIIa inhibitors, and Factor Xa inhibitors. Prepn. of a sterol inhibitor ezetimibe is described.

L8 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:391768 HCAPLUS
DN 136:382014
TI Artery and vein smooth muscle-specific Ephrin family of ligands as molecular markers and uses
IN Anderson, David J.; Garcia-Cardena, Guillermo; Gimbrone, Michael A., Jr.; Wang, Hai U.
PA California Institute of Technology, USA; The Brigham and Women's Hospital, Inc.
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002040540	A2	20020523	WO 2001-US42961	20011120
	WO 2002040540	A3	20030116		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002032405	A5	20020527	AU 2002-32405	20011120
	US 2002136726	A1	20020926	US 2001-988496	20011120
	EP 1337276	A2	20030827	EP 2001-991925	20011120
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-252009P	P	20001120		
	WO 2001-US42961	W	20011120		

AB The present invention relates to methods of distinguishing and sepg. arterial cells from venous cells, and more specifically, distinguishing and sepg. arterial smooth muscle cells from venous smooth muscle cells based on their resp. mol. markers; methods of selectively targeting or delivering agents, drugs, nucleic acids and/or gene products to arteries (and in particular to arterial smooth muscle cells) or veins; methods of altering (enhancing or inhibiting, where inhibiting includes partially or completely inhibiting) the function of artery-specific or vein-specific mol. markers or interaction between them (and, thus, enhancing or inhibiting the effect such functions or interactions have on arterial smooth muscle cells or venous smooth muscle cells); and methods of screening for drugs which act selectively on arterial cells (and more specifically, on arterial smooth muscle cells) or venous cells (and more specifically, on venous smooth muscle cells). In one embodiment the mol. marker is a member of a smooth muscle cell surface ligand-receptor pair which is differentially expressed on arterial and venous smooth muscle cells. For example, as described in detail herein, a member of the Ephrin family of ligands is a mol. marker for arterial smooth muscle cells and can be used to distinguish or isolate arterial smooth muscle cells. Expression of EphrinB2 in arterial cells (e.g., arterial endothelial cells, arterial smooth muscle cells) can be used to advantage in methods for targeting agents and/or encoded polypeptides to arterial smooth muscle cells, altering angiogenesis, assessing the effect of agents on arterial smooth muscle cells, identifying arterial smooth muscle cells, isolating arterial smooth muscle cells and prodn. of artificial vessels, for example. Protein. The transmembrane ligand ephrinB2 and its receptor tyrosine kinase EphB4 are mol. markers of embryonic arterial and venous endothelial cells, resp., and are essential for angiogenesis. Here the authors show that expression of ephrinB2 persists in adult arteries where it extends into some of the smallest diam. microvessels, challenging the classical view that capillaries have neither arterial nor venous identity. EphrinB2 also identifies arterial microvessels in several settings of adult neovascularization, including tumor angiogenesis, contravening the dogma that tumor vessels arise exclusively from postcapillary venules. Unexpectedly, expression of ephrinB2 also defines a stable genetic difference between arterial and venous vascular smooth muscle cells. These observations argue for revisions of classical concepts of capillary identity and the topog. of neovascularization. They also imply that ephrinB2 may be functionally important in neovascularization and in

arterial smooth muscle, as well as in embryonic angiogenesis.

L8 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:31759 HCAPLUS
DN 136:96052
TI Methods for detecting activity of clotting factors
IN Nelsestuen, Gary L.
PA Regents of the University of Minnesota, USA
SO PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002003075	A2	20020110	WO 2001-US20307	20010626
	WO 2002003075	A3	20021227		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6423826	B1	20020723	US 2000-607716	20000630
	US 2003211460	A1	20031113	US 2002-312685	20021230
PRAI	US 2000-607716	A1	20000630		
	WO 2001-US20307	W	20010626		

AB Whole blood assays and kits are described for evaluating dosage of factor VIIa or activated protein C, as well as for monitoring responsiveness to factor VIIa or activated protein C. The invention discloses the use of blood coagulation factors for treatment of hemophilia.

L8 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:568202 HCAPLUS
DN 135:163357
TI Expression of human codon modified DAF gene in mammalian cells for reducing transplant rejection
IN Miyagawa, Shuji
PA Nippon Meat Packers, Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001211882	A2	20010807	JP 2000-22784	20000131
PRAI	JP 2000-22784		20000131		

AB This invention provides codon modified human complement decay-accelerating factor (DAF) gene which was expressed in transgenic mouse. The codon modification of transplant related genes is used to increase the expression of these genes in discordant transplant donor to reduce rejection reaction during transplants. The method described in this invention can be used to rejection reaction, blood coagulation and reperfusion of hypoemia.

L8 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:564887 HCAPLUS
DN 135:142255
TI Drug delivery systems for treatment of restenosis and anastomotic intimal hyperplasia
IN Helmus, Michael N.; Cunanan, Crystal; Tremble, Patrice
PA Edwards Lifesciences Corporation, USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001054748	A1	20010802	WO 2001-US2563	20010125
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,				

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002026236	A1	20020228	US 2001-771480	20010125
US 6730313	B2	20040504		
EP 1250166	A1	20021023	EP 2001-905081	20010125

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003520830	T2	20030708	JP 2001-554731	20010125
PRAI US 2000-178087P	P	20000125		
WO 2001-US2563	W	20010125		

AB The invention provides methods for treating injuries to 1 or more internal structures of a subject by administering a drug delivery vehicle to an external surface of the injured structure. The drug delivery vehicle substantially adheres to the site of administration and provides for the release of a bioactive agent that reduces or prevents further injury to the internal structure by disease processes, such as hyperplasia. Thus, a fibrin polymer formulation, polymd. from a mixt. contg. a final concn. of 25-30 mg/mL fibrinogen, 5 IU human factor XIII, 50 IU human thrombin, and paclitaxel was prepd. Also, each vial of paclitaxel formulated in delayed-release microspheres was reconstituted with 4 mL sterile saline, and 2 mL of this mixt. was added per vial of a Sealant Protein Conc. Anal. of the data obtained by angiog. suggested there was no significant difference between control, vehicle and paclitaxel treatment groups.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:564884 HCAPLUS
DN 135:142301
TI Bioactive coatings to prevent tissue overgrowth on artificial heart valves made of polymeric materials
IN Helmus, Michael N.; Cunanan, Crystal; Tremble, Patrice; Kafesjian, Ralph
PA Edwards Lifesciences Corporation, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001054745	A2	20010802	WO 2001-US2621	20010125
WO 2001054745	A3	20011213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1250165	A2	20021023	EP 2001-906708	20010125

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003520645	T2	20030708	JP 2001-554728	20010125
PRAI US 2000-178084P	P	20000125		
US 2000-571987	A	20000516		
WO 2001-US2621	W	20010125		

AB A prosthetic heart valve resistant to tissue overgrowth following implantation comprises a sewing ring and a housing component enclosing a valve component, wherein a member selected from sewing ring, a housing component, and a valve component contains at least one biol. active material in an amt. sufficient to prevent the infiltration of fibrous tissue ("pannus") from the host into the structure of the prosthetic valve. Preventing or decreasing the overgrowth of the prosthetic valve by pannus reduces the complications assocd. with the implantation and use of prosthetic heart valves. The sewing ring comprises a polymeric material selected from plastics, rubbers, or fabrics. The fabric comprises a material selected from thermoplastic polyurethanes, nylons, polypropylene, polytetrafluoroethylene, polyesters, polyether-polyester block copolymers, polyamides, polyimides, polyolefins, synthetic hydrocarbon elastomers, and natural rubber. The biol. active material is selected from a group consisting of antithrombotics, antiinflammatories, corticosteroids,

antimicrotubule agents, antisense oligonucleotides, antineoplastics, ***antioxidants*** , antiplatelets, etc. The artificial heart valve components are at least partially covered with a coating for release of biol. active material in the form of gels, foams, suspensions, microcapsules, solid polymeric support and fibrous structures.

L8 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:447494 HCAPLUS
DN 135:194295
TI Augmentation in expression of activation-induced genes differentiates memory from naive CD4+ T cells and is a molecular mechanism for enhanced cellular response of memory CD4+ T cells
AU Liu, Kebin; Li, Yu; Prabhu, Vinayakumar; Young, Lynn; Becker, Kevin G.; Munson, Peter J.; Weng, Nan-Ping
CS Laboratory of Immunology, National Institute on Aging, National Institutes of Health, Baltimore, MD, 21224, USA
SO Journal of Immunology (2001), 166(12), 7335-7344
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB To understand the mol. basis for the immunol. memory response, the authors have used cDNA microarrays to measure gene expression of human memory and naive CD4+ T cells at rest and after activation. Our anal. of 54,768 cDNA clones provides the first glimpse into gene expression patterns of memory and naive CD4+ T cells at the genome-scale and reveals several novel findings. First, memory and naive CD4+ T cells expressed similar nos. of genes at rest and after activation. Second, the authors have identified 14 cDNA clones that expressed higher levels of transcripts in memory cells than in naive cells. Third, the authors have identified 135 (130 known genes and 5 expressed sequence tags) up-regulated and 68 (42 known genes and 26 expressed sequence tags) down-regulated cDNA clones in memory CD4+ T after in vitro stimulation with anti-CD3 plus anti-CD28. Interestingly, the increase in mRNA levels of up-regulated genes was greater in memory than in naive CD4+ T cells after in vitro stimulation and was higher with anti-CD3 plus anti-CD28 than with anti-CD3 alone in both memory and naive CD4+ T cells. Finally, the changes in expression of actin and cytokine genes identified by cDNA microarrays were confirmed by Northern and protein analyses. Together, the authors have identified .apprx.200 cDNA clones whose expression levels changed after activation and suggest that the level of expression of up-regulated genes is a mol. mechanism that differentiates the response of memory from naive CD4+ T cells.
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:333762 HCAPLUS
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032928	A2	20010510	WO 2000-US30474	20001103
	WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	US 1999-165398P	P	19991105
	US 2000-196571P	P	20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of

multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

L8 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:128363 HCAPLUS
DN 126:223389
TI Regulation of tissue factor initiated thrombin generation by the stoichiometric inhibitors ***tissue*** ***factor*** ***pathway*** ***inhibitor*** , antithrombin-III, and heparin cofactor-II
AU van 't Veer, Cornelis; Mann, Kenneth G.
CS Dep. Biochem., Univ. Vermont, Berlington, VT, 05405-0068, USA
SO Journal of Biological Chemistry (1997), 272(7), 4367-4377
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The effect of the stoichiometric inhibitors ***tissue*** ***factor*** ***pathway*** ***inhibitor*** (TFPI), antithrombin-III (AT-III) and heparin cofactor-II (HC-II) on thrombin generation were evaluated in a reaction system composed of coagulation factors VIIa, X, IX, VIII, and V and prothrombin initiated by tissue factor (TF) and phospholipids. Initiation of the reaction in the absence of inhibitors resulted in explosive thrombin generation for factor VIIa.cntdot.TF concns. varying from 100 to 0.25 pM with the lag time or initiation phase of thrombin generation increasing from 0 to 180 s with decreasing factor VIIa.cntdot.TF concns. During the propagation phase, prothrombin is quant. activated to 1.4 .mu.M .alpha.-thrombin. At normal plasma concn. (2.5 nM) full-length recombinant TFPI prolonged the initiation phase of thrombin generation 2-fold, and the rate of thrombin generation in the propagation phase of the reaction was 25-50% that of the uninhibited reaction when the reaction was initiated with 1.25-20 pM factor VIIa.cntdot.TF. Inhibition of the reaction by TFPI is assocd. with a delay in factor V activation. In the presence of TFPI no explosive thrombin generation was obsd. when factor VIII was omitted from reactions initiated by factor VIIa.cntdot.TF concns. .ltoreq. 20 pM. This indicates that in the presence of TFPI the factor IXa.cntdot.factor VIIIa pathway becomes essential at low factor VIIa.cntdot.TF concns. In the reconstituted system, AT-III (3.4 .mu.M) did not prolong the initiation phase of thrombin generation when the reaction was initiated with 1.25 .mu.M factor VIIa.cntdot.TF, nor did AT-III delay factor V activation. The rate of thrombin formation in the presence of AT-III was reduced to 30% that of the uninhibited reaction, and the .alpha.-thrombin formed was rapidly inhibited subsequent to its generation. The addn. of HC-II alone at its physiol. concn. (1.38 .mu.M) to the procoagulant mixt. did not alter the rate or extent of thrombin generation. Subsequently, the thrombin formed was slowly inhibited by HC-II. The slow inactivation of thrombin by HC-II does not contribute to thrombin inhibition in the presence of AT-III. In the contrast, the combination of physiol. levels of AT-III and TFPI inhibited explosive thrombin generation initiated by 1.25 pM factor VIIa.cntdot.TF completely. The absence of prothrombin consumption indicated that the combination of TFPI and AT-III is able to prevent the formation of prothrombinase activity at low factor VIIa.cntdot.TF concns. The data indicate that TFPI potentiates the action of AT-III by decreasing the rate of formation and thus the amt. of catalyst formed in the reaction, enabling AT-III to effectively ***scavenge*** the limited traces of factor IXa and factor Xa formed in the presence of TFPI. The initiation of thrombin generation by increasing factor VIIa.cntdot.TF concns. in the presence of physiol. concns. of TFPI and AT-III showed dramatic changes in the maximal rates of thrombin generation over small changes in initiator concn. These data demonstrate that significant thrombin generation becomes a "threshold limited" event with regard to the initiating factor VIIa.cntdot.TF concn. in the presence of TFPI and AT-III.

L8 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:677610 HCAPLUS
DN 121:277610
TI Studies on the inflammatory-coagulant axis in the baboon response to E.coli: Regulatory roles of proteins C, S, C4bBP and of inhibitors of tissue factor.
AU Taylor, Fletcher B. Jr.
CS Cardiovascular Biology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA
SO Progress in Clinical and Biological Research (1994), 388(BACTERIAL ENDOTOXINS), 175-94
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal; General Review
LA English
AB A review with 13 refs. The baboon model of E. coli sepsis illustrates three concepts with respect to the host response and vascular endothelium. First, the endothelium is the primary target. E. coli sepsis is an acute inflammatory disease of the vascular endothelium. Second, the endothelium is not a passive target. Initially it regulates both the inflammatory and coagulopathic aspects of E. coli sepsis through membrane assocd. regulatory receptor/plasma protein assemblies including protein C/thrombomodulin, activated protein C/protein S, C4bBP/protein S, ***tissue*** ***factor*** ***pathway*** ***inhibitor*** /Xa, antithrombin III/glycosaminoglycans. Third, when overridden by inflammatory events, the endothelium can change its anticoagulant phenotype and mount a massive procoagulant fibrinolytic counter-attack on its luminal side through the expression of tissue factor and release of tissue plasminogen activator. Fourth, again when overridden by inflammatory events, the endothelium can change its ***antioxidant*** phenotype and produce a "distal" tissue hypoxia on its adluminal side through induction of free radical generation and peroxidn. of mitochondrial lipid membranes of those tissues with high metabolic rates. It has become increasingly clear that the so-called anticoagulant systems which act on the proximal factors of the clotting cascade (protein C, TFPI, AT-III, PGI2) also attenuate the amplification of the inflammatory response. Aspects of the mechanism by which this occurs are coming to light. This includes the attenuation of IL-6 response by TFPI and the attenuation of the complement effects by C4bBP/PS. The specifics of these observations in the E. coli sepsis model will be reviewed.

=> file uspatfull uspat2
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	58.08	211.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-14.00	-14.00

FILE 'USPATFULL' ENTERED AT 11:05:42 ON 02 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 11:05:42 ON 02 SEP 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> s l3(l)l4 and pd<20030108
PROXIMITY OPERATION NOT ALLOWED
Certain operators may not be nested in combination with other operators. A nested operator is valid only when it occurs at the same level or above the operator outside the nested phrase as determined by the following precedence list:

1. Numeric
2. (W), (NOTW), (A), (NOTA)
3. (S), (NOTS)
4. (P), (NOTP)
5. (L), (NOTL)
6. AND, NOT
7. OR

For example, '(MONOCLONAL(W)ANTIBOD?)(L)ANTIGEN?' is valid since (W) is above (L) on the precedence list. However, '((THIN(W)LAYER)(L)PHOSPHOLIPID#)(A)LACTONE#' is not valid since (L) is below (A) on the precedence list. The only exception is the 'OR' operator. This operator may be used in combination with any other operator. For example, '(ATOMIC OR NUCLEAR)(W)REACTOR' is valid.

```
=> s l3(l)l2 and pd<20030108
L9          170 L3(L) L2 AND PD<20030108

=> s l3(5a)l2 and pd<20030108
L10           4 L3(5A) L2 AND PD<20030108

=> s l3(10a)l2 and pd<20030108
L11           5 L3(10A) L2 AND PD<20030108

=> d cbib hit

L11  ANSWER 1 OF 5  USPATFULL on STN
2002:291062 Secreted protein HNFGF20.
    Komatsoulis, George, Silver Spring, MD, United States
    Rosen, Craig A., Laytonsville, MD, United States
    Ruben, Steven M., Olney, MD, United States
    Duan, Roxanne D., Bethesda, MD, United States
    Moore, Paul A., Germantown, MD, United States
    Shi, Yanggu, Gaithersburg, MD, United States
    LaFleur, David W., Washington, DC, United States
    Wei, Ying-Fei, Berkeley, CA, United States
    Ni, Jian, Rockville, MD, United States
    Florence, Kimberly A., Rockville, MD, United States
    Young, Paul, Gaithersburg, MD, United States
    Brewer, Laurie A., St. Paul, MN, United States
    Soppet, Daniel R., Centreville, VA, United States
    Endress, Gregory A., Potomac, MD, United States
    Ebner, Reinhard, Gaithersburg, MD, United States
    Olsen, Henrik, Gaithersburg, MD, United States
    Mucenski, Michael, Cincinnati, OH, United States
    Human Genome Sciences, Inc., Rockville, MD, United States (U.S.
    corporation)
    US 6476195 B1 20021105
    APPLICATION: US 2000-489847  20000124 (9)
    PRIORITY: US 1998-94657P  19980730 (60)
    US 1998-95486P  19980805 (60)
    US 1998-96319P  19980812 (60)
    US 1998-95454P  19980806 (60)
    US 1998-95455P  19980806 (60)
    DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d cbib hit 2-5

L11  ANSWER 2 OF 5  USPATFULL on STN
2002:250788 Artery smooth muscle- and vein smooth muscle-specific proteins and
    uses therefor.
    Anderson, David J., Atladena, CA, UNITED STATES
    Garcia-Cardena, Guillermo, Boston, MA, UNITED STATES
    Gimbrone, Michael A., JR., Jamaica Plain, MA, UNITED STATES
    Wang, Hai U., Eldorado Hills, CA, UNITED STATES
    California Institute of Technology, Pasadena, CA (U.S. corporation)
    US 2002136726 A1 20020926                                          <--
    APPLICATION: US 2001-988496  A1  20011120 (9)
    PRIORITY: US 2000-252009P  20001120 (60)
    DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI     US 2002136726      A1   20020926                                <--
CLM    What is claimed is:
       8. The method of claim 1 wherein said agent is selected from the group
       consisting of a cyclin G1 mutant polypeptide, a p27-p16 chimeric
       polypeptide, a hepatocyte growth factor, a herpes simplex virus
       thymidine kinase polypeptide, a cytosine deaminase-5-flurocytosine
       polypeptide, a non-phosphorylatable retinoblastoma polypeptide, a
       chimeric pRb2/p130 polypeptide, a p21 polypeptide, a p27 polypeptide, a
       p53 polypeptide, a dominant negative H-ras polypeptide, an eNOS
       polypeptide, an iNOS polypeptide, a synthetic double-stranded nucleic
       acid with high binding affinity for E2F, an anti-sense oligonucleotide
       to p65, an anti-sense oligonucleotide to basic fibroblast growth factor,
       an active site inactivated factor VIIa polypeptide, a recombinant
         ***tissue***     ***factor***     ***pathway***     ***inhibitor***  ,
       rapamycin, an   ***antioxidant***  , a glycoprotein IIb/IIIa receptor
       antagonist, a calcium channel blocker and a nitric oxide donor.
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L11 ANSWER 3 OF 5 USPATFULL on STN
2002:175279 186 human secreted proteins.
Ruben, Steven M., Olney, MD, United States
Rosen, Craig A., Laytonsville, MD, United States
Fischer, Carrie L., Burke, VA, United States
Soppet, Daniel P., Centreville, VA, United States
Carter, Kenneth C., North Potomac, MD, United States
Bednarik, Daniel R., Columbia, MD, United States
Endress, Gregory A., Potomac, MD, United States
Yu, Guo-Liang, Berkeley, CA, United States
Ni, Jian, Rockville, MD, United States
Feng, Ping, Gaithersburg, MD, United States
Young, Paul E., Gaithersburg, MD, United States
Greene, John M., Gaithersburg, MD, United States
Ferrie, Ann M., Tewksbury, MA, United States
Duan, Roxanne, Bethesda, MD, United States
Hu, Jing-Shan, Sunnyvale, CA, United States
Florence, Kimberly A., Rockville, MD, United States
Olsen, Henrik S., Gaithersburg, MD, United States
Ebner, Reinhard, Gaithersburg, MD, United States
Brewer, Laurie A., St. Paul, MN, United States
Moore, Paul A., Germantown, MD, United States
Shi, Yanggu, Gaithersburg, MD, United States
Lafleur, David W., Washington, DC, United States
Li, Yi, Sunnyvale, CA, United States
Zeng, Zhizhen, Lansdale, PA, United States
Kyaw, Hla, Frederick, MD, United States
Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
US 6420526 B1 20020716
APPLICATION: US 1998-149476 19980908 (9)
PRIORITY: US 1997-40162P 19970307 (60)
US 1997-40333P 19970307 (60)
US 1997-38621P 19970307 (60)
US 1997-40626P 19970307 (60)
US 1997-40334P 19970307 (60)
US 1997-40336P 19970307 (60)
US 1997-40163P 19970307 (60)
US 1997-47600P 19970523 (60)
US 1997-47615P 19970523 (60)
US 1997-47597P 19970523 (60)
US 1997-47502P 19970523 (60)
US 1997-47633P 19970523 (60)
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US 1997-47581P 19970523 (60)
US 1997-47584P 19970523 (60)
US 1997-47500P 19970523 (60)
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US 1997-47492P 19970523 (60)
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US 1997-47601P 19970523 (60)
US 1997-43580P 19970411 (60)
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US 1997-43313P 19970411 (60)
US 1997-43672P 19970411 (60)
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US 1997-48974P 19970606 (60)
US 1997-56886P 19970822 (60)
US 1997-56877P 19970822 (60)
US 1997-56889P 19970822 (60)
US 1997-56893P 19970822 (60)

US 1997-56630P 19970822 (60)
US 1997-56878P 19970822 (60)
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US 1997-47589P 19970523 (60)
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US 1997-47614P 19970523 (60)
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US 1997-43576P 19970411 (60)
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US 1997-43670P 19970411 (60)
US 1997-56632P 19970822 (60)
US 1997-56664P 19970822 (60)
US 1997-56876P 19970822 (60)
US 1997-56881P 19970822 (60)
US 1997 6909P 19970822 (60)
US 1997 6875P 19970822 (60)
US 1997- 6862P 19970822 (60)
US 1997 6887P 19970822 (60)
US 1997 6908P 19970822 (60)
US 1997 8964P 19970606 (60)
US 1997 7650P 19970905 (60)
US 1997-56884P 19970822 (60)
US 1997-57669P 19970905 (60)
US 1997-49610P 19970613 (60)
US 1997-61060P 19971002 (60)
US 1997-51926P 19970708 (60)
US 1997-52874P 19970716 (60)
US 1997-58785P 19970912 (60)
US 1997-55724P 19970818 (60)
US 1997-40161P 19970307 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 4 OF 5 USPATFULL on STN
2002:19393 Secreted protein HLHFP03.
Rosen, Craig A., Laytonsville, MD, United States
Ruben, Steven M., Olney, MD, United States
Olsen, Henrik S., Gaithersburg, MD, United States
Ebner, Reinhard, Gaithersburg, MD, United States
Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
US 6342581 B1 20020129
APPLICATION: US 1999-227357 19990108 (9)
PRIORITY: US 1997-58785P 19970912 (60)
US 1997-58664P 19970912 (60)
US 1997-58660P 19970912 (60)
US 1997-58661P 19970912 (60)
US 1997-55722P 19970818 (60)
US 1997-55723P 19970818 (60)
US 1997-55948P 19970818 (60)
US 1997-55949P 19970818 (60)
US 1997-55953P 19970818 (60)
US 1997-55950P 19970818 (60)

US 1997-55947P 19970818 (60)
US 1997-55964P 19970818 (60)
US 1997-56360P 19970818 (60)
US 1997-55684P 19970818 (60)
US 1997-55984P 19970818 (60)
US 1997-55954P 19970818 (60)
US 1997-51926P 19970708 (60)
US 1997-52793P 19970708 (60)
US 1997-51925P 19970708 (60)
US 1997-51929P 19970708 (60)
US 1997-52803P 19970708 (60)
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US 1997-51931P 19970708 (60)
US 1997-51932P 19970708 (60)
US 1997-51916P 19970708 (60)
US 1997-51930P 19970708 (60)
US 1997-51918P 19970708 (60)
US 1997-51920P 19970708 (60)
US 1997-52733P 19970708 (60)
US 1997-52795P 19970708 (60)
US 1997-51919P 19970708 (60)
US 1997-51928P 19970708 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 5 OF 5 USPATFULL on STN
2001:107647 Human antibodies that bind human TNF.alpha..
Salfeld, Jochen G., North Grafton, MA, United States
Allen, Deborah J., Cambridge, United Kingdom
Hoogenboom, Hendricus R. J. M., Hertogsingel, MA, United States
Kaymakcalan, Zehra, Westboro, MA, United States
Labkovsky, Boris, Framingham, MA, United States
Mankovich, John A., Andover, MA, United States
McGuinness, Brian T., Comberton, United Kingdom
Roberts, Andrew J., Cambridge, United Kingdom
Sakorafas, Paul, Newton, MA, United States
Schoenhaut, David, Garfield, NJ, United States
Vaughan, Tristan J., Impington, United Kingdom
White, Michael, Framingham, MA, United States
Wilton, Alison J., Cambridge, United Kingdom
BASF Aktiengesellschaft, Rheiland-Pfalz, Germany, Federal Republic of (non-U.S. corporation)
US 6258562 B1 20010710
WO 9729131 19970814 <--
APPLICATION: US 1999-125098 19990316 (9) <--
WO 1997-US2219 19970210 19990316 PCT 371 date 19990316 PCT 102(e) date
PRIORITY: US 1996-31476P 19961125 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6258562 B1 20010710
WO 9729131 19970814 <--
DETD Nonlimiting examples of therapeutic agents for sepsis with which an antibody, or antibody portion, of the invention can be combined include the following: hypertonic saline solutions; antibiotics; intravenous gamma globulin; continuous hemofiltration; carbapenems (e.g., meropenem); antagonists of cytokines such as TNF.alpha., IL-.beta., IL-6 and/or IL-8; CDP-571BAY-10-3356 (humanized anti-TNF.alpha. antibody; Celltech/Bayer); cA2 (chimeric anti-TNF.alpha. antibody; Centocor); 75 kdTNFR-IgG (75 kD TNF receptor-IgG fusion protein; Immunex; see e.g., Arthritis & Rheumatism (1994) Vol. 37, S295; J Invest. Med. (1996) Vol. 44, 235A); 55 kdTNFR-IgG (55 kD TNF receptor-IgG fusion protein; Hoffmann-LaRoche); Cytokine Regulating Agents (CRAs) HP228 and HP466 (Houghten Pharmaceuticals, Inc.); SK&F 107647 (low molecular peptide; SmithKline Beecham); tetravalent guanylhydrazone CNI-1493 (Picower Institute); ***Tissue*** ***Factor*** ***Pathway*** ***Inhibitor*** (TFPI; Chiron); PHP (chemically modified hemoglobin; APEX Bioscience); iron ***chelators*** and chelates, including diethylenetriamine pentaacetic acid--iron (III) complex (DTPA iron (III); Molichem Medicines); lisofylline (synthetic small molecule methylxanthine; Cell Therapeutics, Inc.); PGG-Glucan (aqeuous soluble .beta.1,3glucan; Alpha-Beta Technology); apolipoprotein A-1 reconstituted with lipids; chiral hydroxamic acids (synthetic antibacterials that inhibit lipid A biosynthesis); anti-endotoxin antibodies; E5531 (synthetic lipid A antagonist; Eisai America, Inc.); rBPI.sub.21 (recombinant N-terminal fragment of human Bactericidal/Permeability-Increasing Protein); and Synthetic Anti-Endotoxin Peptides (SAEP; Bios Ynth Research Laboratories);

=> log y
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.89	227.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-14.00

STN INTERNATIONAL LOGOFF AT 11:09:56 ON 02 SEP 2004